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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: 02/21/2008

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

SUBJECT: Pyraclostrobin: Human Health Risk Assessment for Proposed Uses on Oats, Oilseed Group (Canola & Flax), Plus Seed Treatment on Oats, Canola, and Flax; Tropical Fruits (Avocado, Black Sapote, Canistel, Mamey Sapote, Mango; Papaya, Sapodilla, & Star Apple); Increased Tolerance on Barley; Adding Aerial Application to Turf & Ornamentals; and Adding In-Furrow Applications to Corn, Soybean, and Sugar Beets. PC Code: 099100, Petition Nos.: 6F7105, 6E7165 and 7E7245. DP Barcodes 334535, 336189, 342971, 342585, 340585.

Regulatory Action: Registration Action New Section 3 Uses
Risk Assessment Type: Single Chemical Aggregate

FROM: Barry O'Keefe, Risk Assessor/Senior Biologist B. O'Keefe
Kelly O'Rourke, Biologist Kelly M. O'Rourke
Registration Action Branch 3
Health Effects Division (7509P)
AND
Jerry Stokes, Chemist Susan V. Hummel, for
Re-Registration Branch 4
Health Effects Division (7509P)
AND
Shelia Piper, Chemist Sheila Piper
Alternative Risk Integration Assessment (ARIA) Team
Risk Integration Minor Use & Emergency Response Branch (RIMUERB)
Registration Division (7505)

THROUGH: Paula Deschamp, Branch Chief
Registration Action Branch 3
Health Effects Division (7509P)

TO: Barbara Madden, Team Leader
Minor Use, Inerts and Emergency Response Branch (MUIERB)
Registration Division (RD) (7505P)
AND
John Bazuin/Tony Kish, PM Team 22
Fungicide Branch
Registration Division (RD) (7505P)

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The Registration Division (RD) of the Office of Pesticide Programs (OPP) has requested that HED evaluate toxicology and residue chemistry data and conduct dietary, aggregate, and occupational exposure and risk assessments, as needed, to estimate the risk to human health that will result from existing and proposed uses of pyraclostrobin.

BASF Corporation submitted a petition (6F7205) requesting the establishment of pyraclostrobin tolerances and the addition of new foliar uses on oats, canola, and flax. In addition, the petitioner proposed seed treatment on oats, canola, and flax.

BASF Corporation also submitted a label amendment to add aerial application to a variety of turf and ornamentals onto the Insignia label (EPA Reg. No. 7969-184).

BASF Corporation also submitted a supplemental label to add an in-furrow spray application at planting for corn, soybean and sugar beet onto the Headline® label (EPA Reg. No. 7969-186).

IR-4 submitted a petition (6E7165) requesting the establishment of pyraclostrobin tolerances and new uses on avocado, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, star apple, and fresh herbs on the Pristine® Fungicide label (EPA Reg. No. 7969-199).

IR-4 submitted another petition (7E7245) requesting to increase the tolerance levels for barley commodities, and to revise the barley pre-harvest interval (PHI) on the Headline® label (EPA Reg. No. 7969-186).

The Health Effects Division (HED) has conducted a human health risk assessment for these proposed and changed uses. HED has high confidence in the quality of the toxicology, chemistry and exposure databases used to assess risk from pyraclostrobin.

A summary of the findings and an assessment of human risk resulting from the registered and proposed tolerances for pyraclostrobin are provided in this document. The risk assessment was provided by Barry O'Keefe (RAB3), the residue chemistry data review by Jerry Stokes (RRB4), the dietary risk assessment by Sheila Piper (ARIA/RIMUERB), and the occupational/residential exposure assessment by Kelly O'Rourke (RAB3).

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1.0 Executive Summary

Pyraclostrobin [carbamic acid, [2-[[[1-(4-chlorophenyl)-1*H*-pyrazol-3-yl]oxy]methyl] phenyl]methoxy-, methyl ester] (CAS nomenclature) belongs to the strobilurin class of fungicides (β-methoxyacrylate class of compounds). Strobilurins are synthetic analogs of a natural antifungal substance which inhibit spore germination, mycelial growth, and sporulation of the fungus on the leaf surface.

Pyraclostrobin is currently registered on barley, berries, *Brassica* vegetables, bulb vegetables, citrus, corn (field, pop and sweet), cotton, cucurbit vegetables, fruiting vegetables, grapes, grass grown for seed, hops, leafy vegetables, legumes (dried peas and beans, succulent shelled peas and beans), mint, peanuts, pistachios, pome fruit, potatoes, root vegetables, rye, soybean, strawberries, stone fruits, sugar beets, sunflower, tuberous and corm vegetables, tree nuts, and wheat, as well as residential and golf course turf. The formulated end use products evaluated in this assessment are labeled under the trade names Headline® (EPA Reg. No. 7969-186), Pristine® Fungicide (EPA Reg. No. 7969-199), Insignia® (EPA Reg. No. 7969-184), and BAS 500 ST (EPA File Symbol 7969-EUN). Pristine® Fungicide (EPA Reg. No. 7969-199) is a dual active ingredient product containing pyraclostrobin and boscalid. Proposed uses/tolerances for boscalid are evaluated in a separate assessment.

BASF Corporation submitted a petition (6F7105) requesting the establishment of tolerances for the combined residues of the fungicide pyraclostrobin and its desmethoxy metabolite, expressed as parent compound, in/on the following commodities: oats grain at 1.0 ppm; oats, hay at 17 ppm; oats, straw at 17 ppm; and oilseed, group 20 at 0.4 ppm. Concurrently, BASF Corp. wishes to amend the product label for Headline® Fungicide (EPA Reg. No. 7969-186), an EC formulation containing 23.6% ai (2.09 lb/gal) pyraclostrobin, to add new foliar uses on oats, canola, and flax. Headline® Fungicide is proposed for foliar applications at maximum seasonal rates of 0.39 lb ai/A for canola and flax and 0.29 lb ai/A for oats. Proposed applications may be made using ground or aerial equipment. The proposed pre-harvest intervals (PHI) range from 21 days (oilseed crops) to the beginning of flowering stage (oats). In addition, the petitioner wishes to register a supplemental label, BAS 500 ST (EPA File Symbol 7969-EUN), a 20% WDG formulation, for seed treatment on oats, canola, and flax. BAS 500 ST is proposed for seed treatment at rates of 0.005-0.04 lb ai/100 lb seed.

BASF Corporation submitted a label amendment to add aerial application to a variety of turf and ornamentals onto the Insignia label (EPA Reg. No. 7969-184) at a proposed maximum application of 0.5 lb ai/acre and a maximum seasonal of 3.0 lb ai/acre at 10 to 28-day intervals.

BASF Corporation submitted a supplemental label to add an in-furrow spray application at planting for corn, soybean and sugar beet onto the Headline® label (EPA Reg. No. 7969-186) at 0.2 lb ai/acre.

evaluated with the findings of the dose-range finding one-generation reproduction study, there is no need to repeat the two-generation reproduction study. In both the acute and subchronic neurotoxicity studies, there were no indications of treatment-related neurotoxicity.

The CARC classified pyraclostrobin into the category "Not Likely to be Carcinogenic to Humans" based on no treatment-related increase in tumors in both sexes of rats and mice, which were tested at doses that were adequate to assess carcinogenicity, and the lack of evidence of mutagenicity.

A variety of oral toxicity studies were used for the different risk assessment scenarios including the rabbit developmental toxicity study, the acute neurotoxicity study in rats, the rat carcinogenicity study, and the 13-week study in dogs. In addition, the 28-day inhalation study in rats was used for short- and intermediate-term occupational and residential inhalation risk assessments. The endpoints in these studies are well characterized and are the most sensitive among available comparable toxicity studies in other species. All dietary points of departure (i.e., acute and chronic RfDs) are calculated from the respective study's NOAEL after applying a 100-fold safety factor (10 X to account for interspecies extrapolation and 10X for intraspecies variation). For all other scenarios, including dermal, inhalation, and incidental oral, an MOE approach will be used with a Level of Concern (LOC) at 100.

The toxicity data base for pyraclostrobin is adequate for evaluation of the FQPA safety factor. The following acceptable studies are available: 1) developmental toxicity studies in rats and rabbits; and 2) a two-generation reproduction study in rats. This assessment reaffirms previous conclusions that the 10X FQPA safety factor for the protection of infants and children should be removed for all potential exposure scenarios to pyraclostrobin because the database is complete and adequate and there are no residual uncertainties for pre- and/or postnatal toxicity. The doses chosen as quantitative risk estimates are adequately protective for infants and children. Exposure data are complete or are estimated based on data that reasonably account for potential exposures. Based on these data and conclusions, the FQPA Safety Factor can be reduced to 1X.

Drinking Water Exposure Estimates

The Environmental Fate and Effects Division (EFED) reviewed the proposed use rates associated with the Section 3 amended registration requests for the use of pyraclostrobin on oats and oilseed crops (canola and flax), fresh herbs (crop group 19), and tropical fruits (avocado, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple). Additionally, EFED reviewed the proposal to add aerial applications to existing turf and ornamentals use sites and the proposal to add in-furrow use to the existing corn, soybean, and sugar beets use sites.

This drinking water exposure assessment was based on the application of the highest seasonal use rate (proposed or registered) of pyraclostrobin, i.e., the aerial application on turf and ornamentals at 0.5 lbs a.i./acre with 6 maximum seasonal applications at 14 day

IR-4 submitted a petition (6E7165) requesting the establishment of pyraclostrobin tolerances, expressed as parent *per se*, in/on the following commodities: herb subgroup 19A, fresh herb at 30.0 ppm; and tropical fruits each at 0.7 ppm (avocado; black sapote; canistel; mamey sapote; mango; papaya; sapodilla; and star apple). Concurrent with the tolerances proposed above, IR-4 wishes to amend the product label for Pristine® Fungicide (EPA Reg. No. 7969-199) to incorporate new uses on avocado, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, star apple, and fresh herbs. Pristine® Fungicide is a WDG formulation containing multiple active ingredients of pyraclostrobin (12.8%) and boscalid (25.2%). The product is proposed for two foliar applications at a 7 or greater day interval on the above crops at rates up to 0.15 lb ai/A with a 0-day PHI.

IR-4 submitted another petition (7E7245) requesting the establishment of tolerances for the combined residues of the fungicide pyraclostrobin and its desmethoxy metabolite, expressed as parent compound, in/on barley, grain at 1.3 ppm and barley, straw at 9.0 ppm. Concurrently, IR-4 wishes to amend the product label for Headline® Fungicide (EPA Reg. No. 7969-186) to revise the barley PHI from "apply no later than 50% head emergence (Feekes 10.3, Zadok's 55)" to 14 days. The maximum seasonal rate of 0.29 lb ai/A remains the same.

The Health Effects Division (HED) has conducted a human health risk assessment for these proposed and changed uses. HED has high confidence in the quality of the toxicology, chemistry and exposure databases used to assess risk from the use of pyraclostrobin.

Hazard Assessment and Dose Response

The quality of the toxicology database for pyraclostrobin is good and the confidence in the hazard and dose-response assessments is high. The toxicity database for pyraclostrobin is considered complete, and deemed adequate for endpoint selection for exposure risk assessment scenarios and for FQPA evaluation. Please refer to Appendix A for the toxicity profile tables. Please also refer to the previous pyraclostrobin risk assessment document for further extensive details (B. O'Keefe, DP Barcode 343700, 9/7/07). The last risk assessment document included an updated toxicology and hazard evaluation, including results of recently submitted toxicity studies, a new carcinogenicity evaluation, and selection of new study/endpoints for exposure by the inhalation route. As there are no new toxicity data associated with these current actions, the hazard characterization and endpoint selection from the previous risk assessment are applied directly to this action.

Pyraclostrobin has a low to moderate acute toxicity. The main target organs for pyraclostrobin are the upper gastrointestinal tract (mainly the duodenum and stomach), the spleen/hematopoiesis, the immune system, and the liver. In reproductive and developmental studies, there was evidence of increased qualitative susceptibility following in utero exposure in the rabbit, but not in rats. In the two-generation reproduction study, the highest dose tested did not cause maternal systemic toxicity, nor did it elicit reproductive or offspring toxicity. Nonetheless, HED determined that, when

intervals. For surface water, a Tier II drinking water assessment was performed using the PRZM/EXAMS models with index reservoir (IR) scenarios and percent cropped area (PCA) adjustment factors. Concentrations of pyraclostrobin in surface water are not likely to exceed 35.6 µg/L for the peak concentration, 2.3 µg/L for the annual average concentration, and 1.5 µg/L for the 30 year average concentration.

Ground water concentrations were estimated using a Tier I SCI-GROW, which predicts the acute and chronic concentrations of pyraclostrobin in shallow ground water to be 0.02 ppb. Ground water sources were not included in the dietary assessment, as the estimated drinking water concentrations (EDWCs) for this water source are minimal in comparison to surface water.

Dietary Exposure Assessment

Acute and chronic dietary exposure assessments were conducted for the proposed and existing food uses and drinking water inputs. These acute and chronic dietary risk assessments are considered only minimally refined.

The acute analysis was conducted using either tolerance level residues or highest residues derived from field trial data conducted at the maximum application rate and minimum PHI permitted on the proposed or existing labels. For all commodities 100% crop treated was assumed. A limited number of experimentally derived processing factors were used to refine the acute analysis. Of note is that relative contribution from drinking water is minimal. HED concludes that the acute exposure estimates are unlikely to underestimate actual acute exposure.

The chronic dietary assessment was conducted using tolerance level residues for all crops except for apple, grape, head lettuce, leaf lettuce, celery, spinach, orange, pepper and tomato where average residues from crop field trials were used. These field trials represent maximum application rates and minimum PHIs. For all commodities 100% crop treated was assumed. A limited number of experimentally derived processing factors from pyraclostrobin processing studies were used to refine the analysis. Again, the relative contribution from drinking water is minimal. HED concludes that the chronic exposure estimates in this analysis are unlikely to underestimate actual exposure.

Acute and chronic exposures and risks do not exceed HED's level of concern for the U.S. population and for all relevant population subgroups. At the 95th percentile, the acute dietary exposure utilized 1.4% of the aPAD for the general U.S. population and 80% of the aPAD for females 13-49 years old, the most highly exposed population subgroup. The chronic dietary exposure utilized 19% of the cPAD for the general U.S. population and 48% of the cPAD for children 1-2 years old, the most highly exposed population subgroup.

Aggregate Exposure Assessment

There are existing residential uses on turf which contribute to aggregate exposures. Residential and recreational turf applications are applied by professional pest control

operators (PCOs) only, and therefore, residential handler exposures do not occur. There is, however, a potential for exposure to homeowners in residential settings from entering previously treated lawns where children might play and adults might work or play. As a result, risk assessments have been completed for postapplication scenarios. Postapplication short- and intermediate-term dermal and incidental oral exposures are expected to occur from the turf use pattern. Common effects (i.e., decreased body weight gain, food intake, and food efficiency) were seen in the studies selected to evaluate dietary, dermal and incidental oral ingestion exposures; and therefore, route-specific exposures can be aggregated.

Aggregate assessments were conducted for acute and chronic dietary (food + drinking water) exposures. Additionally, short- and intermediate-term aggregate risk assessments were conducted. Both short- and intermediate-term exposures may occur during postapplication activities for adults and children. However, because the toxicity endpoints and points of departure are identical for short- and intermediate-term exposures, separate risk estimates for short- and intermediate-term exposures were not calculated. These short-/intermediate-term aggregate risk assessments take into account average exposure estimates from dietary consumption of pyraclostrobin (food and drinking water) and non-occupational/residential uses (turf); i.e. for toddlers incidental oral, dermal, and average food plus drinking water exposures are aggregated, and for adults, dermal and average food plus drinking water exposures are aggregated.

The total combined MOE from dietary (food + water) and non-occupational/residential exposure is 100 for children 1-2 years old, which is not of concern to HED. For adults the total combined MOE is 200, which also is not of concern to HED. These aggregate exposure risk assessments are considered conservative estimates, that should not underestimate risks, because of the following inputs: 1) dietary inputs primarily used tolerance level residues; 2) crop specific (turf) screening level drinking water modeling data were used (i.e., Tier II surface water model); 3) maximum application rates and minimum application intervals were used; and 4) conservative SOPs and upper level estimates of exposure were employed.

Occupational Handler Exposure Assessment

No chemical-specific handler exposure data were submitted in support of these registrations. For the assessment of the foliar and in-furrow uses, data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 as presented in PHED Surrogate Exposure Guide (8/98) were used. For assessing seed treatment activities, exposure data were taken from HED Science Advisory Council for Exposure Policy 14: Standard Operating Procedures for Seed Treatment and HED Science Advisory Council for Exposure Standard Operating Procedure 15: Amount of Seed Treated or Planted per Day.

Results from the assessment of all occupational handler scenarios indicate that risks are not of concern with baseline clothing, or in some cases, when gloves and respirator are used to mitigate exposure. For foliar treatments, gloves were added for scenarios involving mixing/loading liquids, and a dust/mist respirator was necessary specifically

for the oats use scenario in order to reach an MOE of 100 or greater. For seed treatment activities, gloves were needed for several scenarios, with the addition of a dust/mist respirator for the scenario designated "multiple activity".

The proposed Headline® Fungicide label requires chemical resistant gloves, however, a respirator is not indicated. The proposed BAS 500 ST label is a supplemental label only, and does not provide information regarding personal protective equipment (PPE).

Occupational Postapplication Exposure Assessment

Previously submitted chemical-specific dislodgeable foliar residue (DFR) data and the interim transfer coefficient policy developed by HED's Science Advisory Council for Exposure, which includes proprietary data from the Agricultural Re-entry Task Force (ARTF) database (policy # 3.1), was used in estimating postapplication exposures.

The results of the postapplication exposure and risk assessment indicate that MOEs of 100 are achieved on Day 0 for all scenarios. The pyraclostrobin technical material has been classified in Toxicity Category III for acute dermal, primary eye irritation, and primary skin irritation. Per the Worker Protection Standard (WPS), a 12-hr restricted entry interval (REI) is required for chemicals classified under Toxicity Category III or IV. The proposed labels indicate an REI of 12 hrs, which is in compliance with the WPS.

Recommendations for Tolerances

HED has completed a human health risk assessment for the proposed new uses of the active ingredient pyraclostrobin.

For Petition #6F7105 - Provided that a revised label is submitted that specifies the appropriate 14-day plantback interval restriction for all annual crops that are not registered and a revised Section F is submitted reflecting the recommended tolerances and commodity definitions presented in Table 14, the residue chemistry, toxicological, and occupational databases support the acceptance of a *conditional registration* on oats, canola, and flax, and establishment of permanent tolerances for pyraclostrobin residues of concern in/on the following raw agricultural commodities:

Oat, grain	1.2 ppm
Oat, hay	18 ppm
Oat, straw	15 ppm
Borage, Crambe, Cuphea, Echium, Flax seed, Gold of pleasure, Hare's ear mustard, Lesquerella, Lunaria, Meadowfoam, Milkweed, Mustard seed, Oil radish, Poppy seed, Rapeseed, Sesame, Sweet rocket (rapeseed subgroup)	0.45 ppm
Castor oil plant, Chinese tallowtree, Euphorbia, Evening primrose, Jojoba, Niger seed, Rose hip,	

Safflower, Stokes aster, Sunflower, Tallowwood, Tea oil plant, Vernonia (sunflower subgroup) ..... 0.45 ppm
Cotton (cotton subgroup) ..... 0.45 ppm

The petitioner should submit a revised Section F to propose individual tolerances of 0.45 ppm for all oilseeds in subgroups rapeseed, sunflower, and cotton, as follows: 1) rapeseed (i.e., borage, crambe, cuphea, echium, flax seed, gold of pleasure, hare's ear mustard, lesquerella, lunaria, meadowfoam, milkweed, mustard seed, oil radish, poppy seed, rapeseed, sesame, and sweet rocket); 2) sunflower (i.e., Castor oil plant, Chinese tallowtree, Euphorbia, Evening primrose, Jojoba, Niger seed, Rose hip, Safflower, Stokes aster, Sunflower, Tallowwood, Tea oil plant, Vernonia); and 3) cotton (only entry presently in this subgroup).

Note: The existing tolerances on sunflower at 0.3 ppm and cotton, undelinted seed at 0.3 ppm should be removed from 40 CFR §180.582.

For Petition #7E7245 - Provided that a revised label is submitted that specifies the appropriate 14-day plantback interval restriction for all annual crops that are not registered and a revised Section F is submitted reflecting the recommended tolerances and commodity definitions presented in Table 14, the residue chemistry, toxicological, and occupational databases support the proposed amended use pattern for barley and permanent tolerances for pyraclostrobin residues of concern in/on the following raw agricultural commodities:

Barley, grain ..... 1.4 ppm
Barley, straw ..... 6.0 ppm

For Petition #6E7165 – Provided that a revised label is submitted that specifies the appropriate 14-day plantback interval restriction for all annual crops that are not registered and a revised Section F is submitted, the residue chemistry, toxicological, and occupational databases support the establishment of a *conditional registration* on avocados, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple, and permanent tolerances for pyraclostrobin residues of concern in/on the following raw agricultural commodities:

Avocado ..... 0.6 ppm
Sapote, black ..... 0.6 ppm
Canistel ..... 0.6 ppm
Sapote, mamey ..... 0.6 ppm
Mango ..... 0.6 ppm
Papaya ..... 0.6 ppm
Sapodilla ..... 0.6 ppm
Star Apple ..... 0.6 ppm

Note: HED is in the process of revising the Commodity Definitions listed under 40 CFR §180.1(h) to make the tropical/subtropical fruit avocado a general commodity; see same 6/14/06 memo by B. Schneider. The specific commodities

included in the general definition for avocado include black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple. Until the regulations have been finalized in the Federal Register, separate tolerances are needed for each specific commodity, at the same level as the respective general commodity tolerance.

A withdrawal letter for withdrawal of the fresh herbs section of petition #6E7165 was recently received by OPP from IR-4 (2/6/08). Therefore, at this time HED is not recommending for tolerances on any herbs in the Herbs subgroup 19A.

The petitioner should submit a revised Section F to correct the tolerance residue definition (parent + metabolite) and to make it consistent with the definition listed in 40 CFR §180.582 (a)(1). The revised Section F should also incorporate the recommended tolerances and commodity definitions presented in Table 14.

Recommendations for Field Residue Data

860.1500 Crop Field Trials

The submitted residue data for avocado are inadequate to fulfill data requirements because the field trials were conducted at exaggerated rates (ca 2.6x). Since the submitted data represent an overestimate of the residues expected from the proposed use, HED considers that the tolerance for avocado may need to be reduced. Also, since the proposed use is for late season foliar application, includes a 0-day preharvest interval, and these data are being translated to support a wide number of tropical/subtropical fruits, HED requests that the petitioner provide additional, bridging field trial data (i.e., two to three field trials at the proposed label rate of 2 applications, total 0.3 lb ai/season) as a condition of registration.

Recommendations for Labels

The proposed Headline® Fungicide label requires chemical resistant gloves; however, a respirator is not indicated and is needed for the handler scenario of mixing/loading liquids for aerial application or chemigation.

The proposed BAS 500 ST label is a supplemental label only, and does not provide information regarding personal protective equipment (PPE). Such PPE information should be added to the label. Gloves are needed for several seed treatment scenarios, and a respirator is needed for the multiple activity scenario.

Environmental Justice Considerations

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf).

As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA under the Continuing Survey of Food Intake by Individuals (CSFII) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas postapplication are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

Review of Human Research

This risk assessment relies in part on data from Pesticide Handlers Exposure Database (PHED) studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These studies have been determined to require a review of their ethical conduct, have received that review, and have been determined to be ethical.

2.0 Ingredient Profile

2.1 Summary of Registered/Proposed Uses

Pyraclostrobin is currently registered on barley, berries, *Brassica* vegetables, bulb vegetables, citrus, corn (field, pop and sweet), cotton, cucurbit vegetables, fruiting vegetables, grapes, grass grown for seed, hops, leafy vegetables, legumes (dried peas and beans, succulent shelled peas and beans), mint, peanuts, pistachios, pome fruit, potatoes, root vegetables, rye, soybean, strawberries, stone fruits, sugar beets, sunflower, tuberous and corm vegetables, tree nuts, and wheat, as well as residential and golf course turf.

A summary of the pyraclostrobin end-use products and proposed crop use patterns discussed in this document is listed in Table 1. No rotational crop restrictions are listed on the product labels.

Table 1. Summary of Proposed Directions for Use of Pyraclostrobin.

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Fresh Herbs (including Angelica, Balm, Basil, Borage, Burnet, Chamomile, Catnip, Chervil, Chive, Chinese Chive, Clary, Coriander (leaf), Costmary, Cilantro (leaf), Curry (leaf), Dillweed (fresh and for processing into oil), Horehound, Hyssop, Lavender, Lemongrass, Lovage (leaf), Marigold, Marjoram (*Origanum* spp.), Nasturtium, Parsley, Pennyroyal, Rosemary, Rue, Sage, Summer Savory, Winter Savory, Sweet Bay, Tansy, Tarragon, Thyme, Wintergreen, Woodruff, and Wormwood)						
Foliar Ground, aerial or through sprinkler irrigation	Pristine® Fungicide 12.8% WDG [7969-199]	0.08 - 0.15	2	0.30	0	Begin applications prior to the onset of disease development and repeat applications 7 days later as needed, or alternate with another registered fungicide having a different mode of action.
Avocado, Black Sapote, Canistel, Mamey Sapote, Mango, Papaya, Sapodilla, and Star Apple						
Foliar Ground, aerial or through sprinkler irrigation	Pristine® Fungicide 12.8% WDG [7969-199]	0.15	2	0.30	0	Begin application prior to the onset of disease development and repeat applications 7 days later as needed, or alternate with another registered fungicide having a different mode of action.
Canola and Flax						
Foliar Ground, aerial or through sprinkler irrigation	Headline® Fungicide 23.6% EC (2.09 lb/gal) [7969-186]	0.10	Not specified	0.39	21	Begin applications prior to disease development, and continue on a 7- to 14-day interval if conditions are conducive for disease development. To limit the potential for development of resistance, do not make more than one application before alternating to a fungicide with a different mode of action. May be used with adjuvants.
Seed treatment	BAS 500 ST 20% WDG [7969-EUN]	0.02-0.04 lb ai/100 lb of seed	1	0.04 lb ai/100 lb of seed	N/A	For control of seed and seedling disease caused by *Pythium* spp. on black mustard, crambe, field mustard, flax, Indian mustard, Indian rapeseed, rapeseed (canola), safflower, and sunflower, apply only in conjunction with registered rates of mefenoxam- or metalaxyl-containing seed treatment products.
Oats						
Foliar Ground, aerial or through sprinkler irrigation	Headline® Fungicide 23.6% EC (2.09 lb/gal) [7969-186]	0.15	2	0.29	14 (hay or feed green-chopped oats)	Begin applications prior to disease development, immediately after flag leaf emergence. Apply no later than the beginning of flowering (Feeke's 10.5.to Zadok's 59) stage. May be used with adjuvants.
Seed treatment	20% WDG [7969-EUN]	0.005-0.01 lb ai/100 lb of seed	1	0.01 lb ai/100 lb of seed	N/A	
Barley						
Foliar Ground, aerial or through sprinkler irrigation	Headline® Fungicide 23.6% EC (2.09 lb/gal) [7969-186]	0.15	2	0.29	14 (hay or feed green-chopped barley)	Use limited to the following states: AZ, CO, ID, MT, NV, NM, OR, TX, UT, WA, and WY. Begin applications prior to disease development, immediately after flag leaf emergence. Apply no later than 50% head emergence (Feeke's

Table 1. Summary of Proposed Directions for Use of Pyraclostrobin.

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
						10.3.to Zadok's 55) stage. May be used with adjuvants.
Corn, Soybean and Sugar beet						
In-Furrow	Headline® Fungicide 23.6% EC (2.09 lb/gal) [7969-186]	0.20	1	0.20	N/A	Apply at planting as an in-furrow application by directing the spray into the furrow before seed is covered. Use a minimum volume of 2.5 gal water per acre.
Turf and Ornamentals						
Foliar Aerial application	Insignia® Fungicide 20% WDG [7969-184]	0.28 - 0.5		3.0	N/A	For aerial application, apply in no less than 10 gallons of spray solution per acre. Repeat at 10- to 28-day intervals, depending on disease. Do not apply more than 2 sequential applications. No aerial application in New York state except as permitted under FIFRA Section 24(c).

Conclusions. The field trial data for herbs subgroup 19A and tropical fruits do not reflect the proposed use patterns since they were conducted at exaggerated rates. Additional bridging field trial residue data are required to reflect the proposed label rates. In addition, label revision is required to specify appropriate rotational crop restrictions. Details of label revisions are incorporated in the respective crop section.

2.2 Physical and Chemical Properties

Common Name: Pyraclostrobin

IUPAC Nomenclature: methyl *N*-{2-[1-(4-chlorophenyl)-1*H*-pyrazol-3-yloxymethyl]phenyl}(*N*-methoxy)carbamate

CAS Nomenclature: methyl [2-[[[1-(4-chlorophenyl)-1*H*-pyrazol-3-yl]oxy]methyl]phenyl]methoxycarbamate

CAS Number: 175013-18-0

Chemical Class/Type: β-methoxyacrylate (compound class) / Strobilurin (fungicide class)

Mode of Action: Acts at the cellular level by inhibiting electron transport in the mitochondrial respiratory chain at the cytochrome-bc1 complex; this disrupts the energy producing systems and can lead to the breakdown of the mitochondrial and cytoplasmic membranes.

Impurities of Concern:	The technical grade pyraclostrobin does not contain any impurities or microcontaminants of concern.
Molecular Formula:	$C_{19}H_{18}ClN_3O_4$
Molecular Weight:	387.82
Appearance:	White to light beige solid
Melting Point:	63.7 - 65.2°C
Boiling Point:	N/A
Density:	1.285 g/cm^3 at 20°C
Water Solubility:	2.41 mg/L in deionized water at 20°C 1.9 mg/L in buffer system pH 7 at 20°C 2.3 mg/L in buffer system pH 4 at 20°C 1.9 mg/L in buffer system pH 9 at 20°C
Solvent Solubility:	at 20°C in: acetone (≥160 mg/L); methanol (11 mg/L); 2-propanol (3.1 mg/L); ethyl acetate (≥160 mg/L); acetonitrile (≥76 mg/L); dichloromethane (≥110 mg/L); toluene (≥100 mg/L); n-heptane (0.36 mg/L); 1-octanol (2.4 mg/L); olive oil (2.9 mg/L); DMF (≥62 mg/L).
Vapor Pressure:	2.6 x 10^{-10} hPa (at 20°C); 6.4 x 10^{-10} hPa (at 25°C)
pK_a:	Does not dissociate in water. There are no dissociable moieties.
K_{ow}:	n-Octanol/water partition coefficient (K_{ow}) at room temperature (=K_{ow} of 3.80, pH 6.2; = K_{ow} 4.18, pH 6.5).

3.0 Hazard Characterization/Assessment

3.1 Hazard and Dose-Response Characterization

3.1.1 Database Summary

The quality of the toxicology database for pyraclostrobin is good and the confidence in the hazard and dose-response assessments is high. The toxicity database for pyraclostrobin is considered complete, and deemed adequate for endpoint selection for exposure risk assessment scenarios and for FQPA evaluation.

The most recent risk assessment included an updated toxicology and hazard evaluation, including results of recently submitted toxicity studies, a new carcinogenicity evaluation, and selection of new study/endpoints for exposure by the inhalation route. Please refer to this previous pyraclostrobin risk assessment document for further extensive details (B. O'Keefe, DP Barcode 343700, 9/7/07). Also, please refer to Appendices 2 and 3 of this current risk assessment document for the toxicity profile tables. As there are no new toxicity data associated with these current actions, the hazard characterization and endpoint selection, from the previous risk assessment are applied directly to this action.

Pyraclostrobin has a low to moderate acute toxicity. The main target organs for pyraclostrobin are the upper gastrointestinal tract (mainly the duodenum and stomach), the spleen/hematopoiesis, the immune system, and the liver. In reproductive and developmental studies, there was evidence of increased qualitative susceptibility following in utero exposure in the rabbit, but not in rats. In the two-generation reproduction study, the highest dose tested did not cause maternal systemic toxicity, nor did it elicit reproductive or offspring toxicity. Nonetheless, HED determined that, when evaluated with the findings of the dose-range finding one-generation reproduction study (MRID# 45596210), there is no need to repeat the two-generation reproduction study. In both the acute and subchronic neurotoxicity studies, there were no indications of treatment-related neurotoxicity.

3.1.2 Toxicological Effects

The toxicity profile of pyraclostrobin, including acute toxicities, may be found in Appendices 2 and 3.

Acute Toxicity: Pyraclostrobin has a low to moderate acute toxicity based on its classification in Toxicity Category IV via the oral route, Toxicity Category III by the dermal route, and Toxicity Category II by the inhalation route of exposure. Pyraclostrobin produces moderate eye irritation (Toxicity Category III), is a moderate dermal irritant (Toxicity Category III), and is not a dermal sensitizer (Appendix 2).

Toxicity from Repeated Oral Exposure: Based on findings in repeated dosing oral studies in more than one species, the main target organs for pyraclostrobin are the upper gastrointestinal tract (mainly the duodenum and stomach), the spleen/hematopoietic system, the liver, and the immune system (listed in the order from most to least sensitive). In addition, reduced body weight/gain and feed intake/efficiency are also common findings. In the 90-day dietary rat, mouse, and dog feeding studies, one or more of the following gastrointestinal (GI) changes were noted: thickening of the duodenal wall, duodenum mucosal hypertrophy or hyperplasia, as well as gross and microscopic ulceration/erosion in the glandular stomach. Mucosal hyperplasia in the duodenum was also observed in rats of both sexes after 28-day administration of 500 (42.3/46.6 (M/F) mg/kg/day) and 1500 (120.2/126.3 (M/F) mg/kg/day) ppm pyraclostrobin. The upper GI-tract effects might, at least partly, explain some of the adverse effects on food consumption/utilization, and body weight; all these effects had a similar threshold which was lower than that needed to elicit the other toxic responses.

The liver was a target organ in the 28-day rat and the 90-day rat and mouse dietary feeding studies based on slight to moderate increased relative liver weight in both species and hepatocellular hypertrophy in the rat studies. Liver necrosis was also increased in the two-year rat carcinogenicity study.

Other findings in the rat and mouse 90-day studies included hematopoietic toxicity. In rats, the hematopoietic effects included mild hemolytic anemia accompanied by increased reticulocytes, increased spleen weight, spleen microscopic changes, and increased total leukocytes, neutrophils, and lymphocytes. In mice, there was mild hemolytic anemia accompanied by a large decline (≥50%) in leukocytes (leukopenia), neutrophils, and lymphocytes. The large decline in white blood cell (WBC) populations was accompanied by dose-dependent thymus atrophy and increased lymph node apoptosis.. The incidences of thymus atrophy ranged from 3/10 to 8/10 in each of the top four dose groups of both sexes compared to 0/10 in the control and lowest dose groups; the severity also increased dose-dependently.

Reproductive & Developmental Toxicity: The pre- and post-natal toxicology database for pyraclostrobin includes the rat and rabbit developmental toxicity studies and the two-generation reproduction toxicity study in rats. There was no evidence of increased quantitative or qualitative susceptibility following in utero exposure to rats. The developmental findings of increased incidences of dilated renal pelvis and cervical ribs with no cartilage were seen at a higher dose than that which caused maternal toxicity and these findings were within historical control background incidences; therefore, they are considered developmental variations rather than malformations. In the rabbit developmental toxicity study, there was evidence of qualitative susceptibility; increases in resorptions/litter and post-implantation losses were seen in the presence of maternal toxicity (decreases in body weight gain and food consumption). However, the concern is low for the qualitative susceptibility in the rabbit developmental study because: The developmental effects were seen in the presence of maternal toxicity; there are clear NOAELs for maternal and developmental toxicities; and this endpoint is used for the acute dietary (RfD) for Females+ 13 as well as for short- and intermediate-term dermal risk assessments.

In the two-generation study, there were no adverse maternal systemic toxicity other than a marginal (non-adverse) decrease (<= 5%) in F0 and F1 parental body weights at the high dose of 300 ppm. The F1 and F2 pups of the 300 ppm dose group had slight decreases in body weights during lactation which were explained to be "likely due to the fact that pups start eating food at this time (day 7) along with potentially receiving test compound or its metabolites in mother milk." The findings were not considered adverse in part because of almost total body weight recovery in F1 parental animals during premating, gestation, and lactation. The NOAEL/LOAEL were 300/>300 ppm for parental, reproductive, and offspring toxicities. In the one generation study, the NOAEL/LOAEL were <200/<= 200 ppm based on dose-dependent decrease in F1 pup body weights.

The HIARC decided that, when evaluated with the findings of the dose-range one-generation reproduction study, there is no need to repeat the two-generation reproduction study (document dated 2/10/03, TXR no. 0051553). The HIARC noted that the greater body weight/body weight gain sensitivity in the offspring of the one-generation reproduction study is possibly due to decreased feed intake by treated pups as they start eating solid feed around day 14; this effect was not reproduced in the two-generation toxicity study.

It should be noted that there was some overlap in the magnitude of the body weight decrease in F1 pups at 300 ppm (4-10%), 200 ppm (7-14%), and 400 ppm (11-20%) to the extent possible from two completely different and independent studies. For any end-point, some degree of variation is to be expected between control animals from different studies for different reasons including animal husbandry (e.g., diurnal, seasonal) as well as differences in instruments and people who collect the measurements. This inter-study variation may explain the F1 pup body weight variance and lack of a perfect dose-response among the similar dose levels (300 ppm vs. 200 and 400 ppm) in both studies.

In conclusion, athough no toxicity was seen at 300 ppm (29.0 mg/kg/day) in the two-generation reproduction study, a new study is not required since such a study would be conducted using a much higher dose and would not provide any additional data for risk assessment purposes. The concern with that study is not that it did not test at a low enough dose but the opposite. Further, it should be noted that acute and chronic reference doses for dietary risks as well as doses for non-dietary risks are based on other studies with NOAELs below the high dose in the two generation study.

Neurotoxicity: In both the acute and subchronic neurotoxicity studies, there were no indications of treatment-related neurotoxicity including clinical signs, qualitative or quantitative neurobehavioral effects, brain weight, or gross/microscopic pathology. None of the other guideline studies reported treatment-related effects on any of these parameters. However, there was a large decrease (about 50%) in serum cholinesterase (but not in erythrocyte or brain cholinesterases) among the females in the rat 28- and 90-day dietary studies at relatively large doses (1000/1500 ppm or about 80 - 126 mg/kg/day). This response might require exposure to a relatively high dose since serum cholinesterase (ChE) was not affected at the end of the two-year chronic toxicity feeding study in rats including the top dose of 200 ppm (9.2/12.6 mg/kg/day in males/females). Also, pyraclostrobin does not seem to persist in rat tissues (see following section) which might explain why serum ChE is not affected by a lifetime exposure to a relatively low dose but is depressed following a short-term exposure at a high dose.

Carcinogenicity: The Cancer Assessment Review Committee (CARC) classified pyraclostrobin into the category **"Not Likely to be Carcinogenic to Humans"** based on no treatment-related increase in tumors in both sexes of rats and mice, which were tested at doses that were adequate to assess carcinogenicity, and the lack of evidence of mutagenicity. The CARC concluded that quantification of carcinogenic potential is not required (TXR document no. 0054516, dated 2/15/07).

3.1.3 Dose-response

A variety of oral toxicity studies were used for the different risk assessment scenarios including the rabbit developmental toxicity study, the acute neurotoxicity study in rats, the rat carcinogenicity study, and the 13-week study in dogs. In addition, the 28-day inhalation study in rats was used for short- and intermediate-term occupational and residential inhalation risk assessments. The endpoints in these studies are well characterized and are the most sensitive among available comparable toxicity studies in other species. All dietary points of departure (i.e., acute and chronic RfDs), are calculated from the respective study's NOAEL after applying a 100-fold safety factor (10 X to account for interspecies extrapolation and 10X for intraspecies variation). For all other scenarios, including dermal, inhalation, and incidental oral, an MOE approach will be used with a Level of Concern (LOC) at 100.

The selected point of departure from the acute neurotoxicity study of 300 mg/kg/day for the acute dietary (general population) risk assessment is appropriate because the decreased body weight gain in males occurred during the first week after a single oral high dose of 1000 mg/kg.

The rabbit developmental toxicity study findings are used for endpoint selections for acute dietary (Females 13+) as well as for short- and intermediate-term dermal exposures. For the acute dietary endpoint (Females 13+), the rabbit developmental findings of increased resorptions/post-implantation loss at the LOAEL of 10 mg/kg/day are assumed to occur following a single *in utero* exposure. These effects were dose-dependently increased at the next (high) dose of 20 mg/kg/day. The same study and developmental endpoint are used for short- and intermediate-term dermal exposures after applying a dermal absorption factor of 14%. Additionally, the maternal endpoints of decreased body weight gain and decreased food intake and food efficiency were found at the LOAEL of 10 mg/kg/day. This selection mitigates any concern from the observed developmental toxicity findings in rabbits which are not assessed in the rat dermal toxicity study.

The rat carcinogenicity study findings are used for endpoint selections for chronic dietary and dermal exposures based on findings of decreased body weight/gain and kidney tubular casts/atrophy in both sexes in addition to liver necrosis and stomach lesions in males at the high dose (LOAEL) of 9.2 mg/kg/day. This study has the lowest NOAEL (3.4 mg/kg/day) in the most sensitive species following chronic exposure. The dermal absorption factor of 14% will be applied to the dermal long-term risk scenario.

The short-, intermediate-, and long-term inhalation endpoints are from the 28-day inhalation toxicity study in rats which had dose-dependent adverse findings in the respiratory system and duodenum. The study's oral equivalents NOAEL/LOAEL are 0.23/6.92 mg/kg/day (corresponding to study's air concentration of 0.001/0.03 mg/L air). The findings are well characterized in that the severity, frequency, and location (e.g., along the respiratory tract) are dose-dependent ranging from no effects at the NOAEL of 0.001 mg/L air to severe respiratory effects and death at the highest dose of 0.3 mg/L air.

The short- and intermediate-term incidental oral endpoints are from the 13-week feeding study in dogs. The NOAEL of 5.8 mg/kg/day is based on increased incidence of diarrhea, clinical chemistry changes, duodenum mucosal hypertrophy, and effects on body weight and food intake/efficiency at 13 mg/kg/day (LOAEL). The NOAEL/LOAEL in this study are comparable to the maternal NOAEL/LOAEL (5/10 mg/kg/day) established in the rabbit developmental toxicity study, and the end-point is appropriate for the population of concern (toddlers).

3.2 FQPA Safety Factor for Infants and Children

The toxicity data base for pyraclostrobin is adequate for evaluation of the FQPA safety factor. The following acceptable studies are available: 1) developmental toxicity studies in rats and rabbits; and 2) a two-generation reproduction study in rats. This assessment reaffirms previous conclusions that the 10X FQPA safety factor for the protection of infants and children should be removed for all potential exposure scenarios to pyraclostrobin because the database is complete and adequate and there are no residual uncertainties for pre- and/or postnatal toxicity. The doses chosen as quantitative risk estimates are adequately protective for infants and children. Exposure data are complete or are estimated based on data that reasonably account for potential exposures.

The acute dietary analysis was based on tolerance level or highest residues and 100% crop treated assumptions for all commodities. Experimentally derived processing factors were used for fruit juices and tomato and wheat commodities. The contribution from drinking water is minimal. HED concludes that the acute exposure estimates in this analysis are unlikely to underestimate actual exposure.

The chronic dietary analysis included tolerance level or average residues from field trial data and 100% crop treated assumptions for all commodities. A limited number of experimentally derived processing factors were used for fruit juices and tomato and wheat commodities. The field trials represent maximum application rates and minimum PHIs. The contribution from drinking water is minimal. HED concludes that the chronic exposure estimates in this analysis are unlikely to underestimate actual exposure.

The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.

While there is potential for postapplication residential exposure, the best data and approaches currently available were used in the pyraclostrobin residential assessment. The Agency used the current conservative approaches for residential assessment, many of which include recent upgrades to the SOPs. The Agency believes that the calculated risks represent conservative estimates of exposure because maximum application rates are used to define residue levels upon which the calculations are based. Exposures are unlikely to be under estimated because the assessment was a screening level assessment.

Based on these data and conclusions, the FQPA Safety Factor can be reduced to 1X.

3.3 Summary of Toxicological Doses and Endpoints for Use in Human Health Risk Assessments

HED recently completed a Section 3 human health risk assessment for the use of pyraclostrobin on cotton and Belgian endive (Memo B. O'Keefe, et. al., 9/7/07, DP# 343700). As there are no new toxicity data associated with this current action, the hazard characterization and endpoint selection, from the previous risk assessment are applied directly to this action. All previous exposure risk assessments remain unchanged. Below are the up-to-date tables.

Table 2. Summary of Toxicological Doses and Endpoints for Pyraclostrobin for Use in Dietary and Non-Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty/F QPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General Population, including Infants and Children)	NOAEL= 300 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Acute RfD = 3.0 mg/kg/day aPAD = 3.0 mg/kg/day	Rat Acute Oral Neurotoxicity LOAEL = 1000 mg/kg/day based on decreased body weight gain in males.
Acute Dietary (Females 13-49 years of age)	NOAEL = 5.0 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Acute RfD = 0.05 mg/kg/day aPAD = 0.05 mg/kg/day	Rabbit Prenatal Developmental Toxicity LOAEL = 10.0 mg/kg/day based on developmental toxicity findings of increased resorptions.
Chronic Dietary (All Populations)	NOAEL= 3.4 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Chronic RfD = 0.034 mg/kg/day cPAD = 0.034 mg/kg/day	Rat Oral Carcinogenicity LOAEL = 9.2 mg/kg/day based on decreased body weight/body weight gain, kidney tubular casts and atrophy in both sexes; increased incidence of liver necrosis and erosion/ulceration of the glandular- stomach and fore-stomach in males.
Incidental Oral Short-Term (1-30 days)	NOAEL= 5.8 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	13-Week Feeding Dog Study LOAEL = 12.9 mg/kg/day based on increased incidence of diarrhea, clinical chemistry changes, duodenum mucosal hypertrophy, and decreased body weight and food intake/efficiency.
Incidental Oral Intermediate-Term (1-6 months)	NOAEL= 5.8 mg/kg/day	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	13-Week Feeding Dog Study LOAEL = 12.9 mg/kg/day based on increased incidence of diarrhea, clinical chemistry changes, duodenum mucosal hypertrophy, and decreased body weight and food intake/efficiency.
Dermal Short-Term (1-30 days)	Oral study NOAEL = 5.0 mg/kg/day (dermal absorption rate = 14 %)	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Rabbit Prenatal Developmental Toxicity LOAEL = 10.0 mg/kg/day based on developmental toxicity findings of increased resorptions and maternal toxicity based on decreased body weight gain and decreased food intake/efficiency.

Table 2. Summary of Toxicological Doses and Endpoints for Pyraclostrobin for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal Intermediate-Term (1-6 months)	Oral study NOAEL = 5.0 mg/kg/day (dermal absorption rate = 14 %)	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Rabbit Prenatal Developmental Toxicity LOAEL = 10.0 mg/kg/day based on developmental toxicity findings of increased resorptions and maternal toxicity based on decreased body weight gain and decreased food intake/efficiency.
Long-Term Dermal (>6 months)	Oral study NOAEL = 3.4 mg/kg/day (dermal absorption rate = 14 %)	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Rat Oral Carcinogenicity LOAEL = 9.2 mg/kg/day based on decreased body weight/body weight gain, kidney tubular casts and atrophy in both sexes; increased incidence of liver necrosis and erosion/ulceration of the glandular- stomach and fore-stomach in males.
Inhalation Short-Term (1-30 days)	NOAEL= 0.23 mg/kg/day (air concentration = 0.001 mg/L)	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Rat 28-day Inhalation LOAEL = 6.9 mg/kg/day (air concentration = 0.03 mg/L) based on duodenum mucosal hyperplasia and respiratory system findings including alveolar histiocytosis and olfactory atrophy/necrosis in nasal tissue.
Inhalation Intermediate-Term (1-6 months)	NOAEL= 0.23 mg/kg/day (air concentration = 0.001 mg/L)	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Rat 28-day Inhalation LOAEL = 6.9 mg/kg/day (air concentration = 0.03 mg/L) based on duodenum mucosal hyperplasia and respiratory system findings including alveolar histiocytosis and olfactory atrophy/necrosis in nasal tissue.
Inhalation Long-Term (>6 months)	NOAEL= 0.23 mg/kg/day (air concentration = 0.001 mg/L)	UF_A= 10x UF_H= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Rat 28-day Inhalation LOAEL = 6.9 mg/kg/day (air concentration = 0.03 mg/L) based on duodenum mucosal hyperplasia and respiratory system findings including alveolar histiocytosis and olfactory atrophy/necrosis in nasal tissue.
Cancer (oral, dermal, inhalation)	Classification: "Not likely to be Carcinogenic to Humans" based on the absence of significant tumor increases in two adequate rodent carcinogenicity studies.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key date (i.e., lack of a critical study). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Table 3. Summary of Toxicological Doses and Endpoints for Pyraclostrobin for Use in Occupational Human Health Risk Assessments				
Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects

Table 3. Summary of Toxicological Doses and Endpoints for Pyraclostrobin for Use in Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal Short-Term (1-30 days)	NOAEL= 5.0 mg/kg/day (dermal absorption rate = 14 %)	UF_A=10x UF_H=10x	Occupational LOC for MOE = 100	Rabbit Prenatal Developmental Toxicity LOAEL = 10.0 mg/kg/day based on developmental toxicity findings of increased resorptions.
Dermal Intermediate-Term (1-6 months)	Oral study NOAEL = 5.0 mg/kg/day (dermal absorption rate = 14 %)	UF_A= 10x UF_H= 10x	Occupational LOC for MOE = 100	Rabbit Prenatal Developmental Toxicity LOAEL = 10.0 mg/kg/day based on developmental toxicity findings of increased resorptions.
Long-Term Dermal (>6 months)	Oral study NOAEL = 3.4 mg/kg/day (dermal absorption rate = 14 %)	UF_A= 10x UF_H= 10x	Occupational LOC for MOE = 100	Rat Oral Carcinogenicity LOAEL = 9.2 mg/kg/day based on decreased body weight/body weight gain, kidney tubular casts and atrophy in both sexes; increased incidence of liver necrosis and erosion/ulceration of the glandular- stomach and fore-stomach in males.
Inhalation Short-Term (1-30 days)	NOAEL= 0.23 mg/kg/day (air concentration = 0.001 mg/L)	UF_A= 10x UF_H= 10x	Occupational LOC for MOE = 100	Rat 28-day Inhalation LOAEL = 6.9 mg/kg/day (air concentration = 0.03 mg/L) based on duodenum mucosal hyperplasia and respiratory system findings including alveolar histiocytosis and olfactory atrophy/necrosis in nasal tissue.
Inhalation Intermediate-Term (1-6 months)	NOAEL= 0.23 mg/kg/day (air concentration = 0.001 mg/L)	UF_A= 10x UF_H= 10x	Occupational LOC for MOE = 100	Rat 28-day Inhalation LOAEL = 6.9 mg/kg/day (air concentration = 0.03 mg/L) based on duodenum mucosal hyperplasia and respiratory system findings including alveolar histiocytosis and olfactory atrophy/necrosis in nasal tissue.
Inhalation Long-Term (>6 months)	NOAEL= 0.23 mg/kg/day (air concentration = 0.001 mg/L)	UF_A= 10x UF_H= 10x	Occupational LOC for MOE = 100	Rat 28-day Inhalation LOAEL = 6.9 mg/kg/day (air concentration = 0.03 mg/L) based on duodenum mucosal hyperplasia and respiratory system findings including alveolar histiocytosis and olfactory atrophy/necrosis in nasal tissue.
Cancer (oral)	Classification: "Not likely to be Carcinogenic to Humans" based on the absence of significant tumor increases in two adequate rodent carcinogenicity studies.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key date (i.e., lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

3.4 Recommendation for Aggregate Exposure Risk Assessments

As per the FQPA, when there are potential residential exposures to the pesticide, aggregate risk assessment must consider exposures from three major sources: oral, dermal and inhalation exposures. When common toxicity endpoints are selected for these routes of exposure they may be aggregated. Aggregate assessments are required for acute and chronic dietary (food + water) exposures, and short-term residential exposures (i.e., chronic dietary plus incidental oral and dermal exposures).

Residential short-/intermediate-term dermal exposure for adults and toddlers were assessed using the NOAEL (5 mg/kg/day) from the rabbit developmental study. While the developmental effect of increased resorptions is not applicable to toddlers, it should be noted that the maternal NOAEL from this study is also 5 mg/kg/day, and is based on reduced body weight gain, food consumption, and food efficiency at the LOAEL of 10 mg/kg/day; this more relevant endpoint was used to assess toddler dermal exposure. For incidental oral ingestion, exposure was assessed using the endpoint from a 13-week feeding study in the dog. The NOAEL from this study is 5.8 mg/kg/day, based on increased incidence of diarrhea, clinical chemistry changes, duodenum mucosal hypertrophy, and decreased body weight and food intake/efficiency at the LOAEL of 12.9 mg/kg/day. A common effect (i.e., decreased body weight gain, food intake, and food efficiency) was seen in the studies selected to evaluate toddler dermal and incidental oral ingestion exposure; therefore, route-specific MOEs were aggregated for toddlers.

3.5 Endocrine disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, pyraclostrobin may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

4.0 Public Health and Pesticide Epidemiology Data

The Centers for Disease Control (CDC) and Prevention recently reported and described five incident events to the Iowa Department of Public Health (IDPH) of exposures that occurred during aerial applications of pyraclostrobin (MMWR Weekly, 2/4/08, 56(51) pp.1343-1345). IDPH investigated the reports. In one event migrant workers were inadvertently exposed to pyraclostrobin due to pilot error and off-target drift of pyraclostrobin to an adjacent field. The migrant workers experienced symptoms including upper respiratory tract pain or irritation, chest pain, nausea, skin redness, eye pain, weakness, headache, and dizziness. In another event, a crop-dusting pilot suffered first degree burns after being exposed to pyraclostrobin which had spilled after his airplane crashed during takeoff. Another three events also involved acute pesticide poisoning associated with off-target drift of pyraclostrobin from nearby aerial applications. In all five of these cases, symptoms subsided after the exposed persons moved indoors or away from the pyraclostrobin treated fields.

Pyraclostrobin labels that permit aerial applications contain specific label language stating not to apply under circumstances where possible drift may occur and how to reduce drift potential.

5.0 Dietary Exposure/Risk Characterization

Reference: *Pyraclostrobin. Petitions for the Establishment of Permanent Tolerances on: (i) Oat Grain, Hay, and Straw, and Oilseed (Crop Group 20) - PP#6F7105; (ii) Fresh Herbs (Herbs Subgroup 19A), Avocado, Black Sapote, Canistel, Mamey Sapote, Mango, Papaya, Sapodilla, and Star Apple - PP#6E7165; and (iii) Barley Grain and Straw- PP#7E7245. Summary of Analytical Chemistry and Residue Data. DP Numbesr 345965, 348700 & 343754; J. Stokes; 02/12/08.*

5.1 Pesticide Metabolism and Environmental Degradation

5.1.1 Metabolism in Primary Crops

Adequate metabolism studies with pyraclostrobin on grapes, potatoes, and wheat have previously been reviewed (D269668, L. Cheng, 11/28/01) in conjunction with PP#0F06139. The results of these studies indicate that the metabolism of pyraclostrobin is similar in the three crops investigated. The HED Metabolism Assessment Review Committee (MARC) concluded that the nature of the residue in plants is understood (HED Metabolism Committee Decision Memo; D278044, L. Cheng, 10/9/01). For purposes of tolerance setting and risk assessment, the terminal residues of concern in plants consist of pyraclostrobin and its desmethoxy metabolite (BF 500-3).

5.1.2 Metabolism in Livestock

Adequate metabolism studies with pyraclostrobin on ruminants and laying hens were previously reviewed (D269668, L. Cheng, 11/28/01) in conjunction with PP#0F06139. The HED MARC has determined that for purposes of tolerance setting and risk assessment, the residues of concern in livestock commodities consist of pyraclostrobin and its metabolites convertible to 1-(4-chlorophenyl)-1*H*-pyrazol-3-ol and 1-(4-chloro-2-hydroxyphenyl)-1*H*-pyrazol-3-ol (HED Metabolism Committee Decision Memo; D278044, L. Cheng, 10/9/01).

5.1.3 Analytical Methodology

Enforcement Method for Plants

Two adequate methods were proposed for enforcing tolerance for residues of pyraclostrobin and BF 500-3 in/on plant commodities: a LC/MS/MS method (BASF Method D9808), and an HPLC/UV method (BASF Method D9904). The validated method LOQ for both pyraclostrobin and BF 500-3 is 0.02 ppm in all tested plant matrices, for a combined LOQ of 0.04 ppm. Adequate independent method validation and radiovalidation data were submitted for both methods (D269668, 11/28/01, L. Cheng), and both methods were forwarded to ACB/BEAD for a petition method validation (D269850, 11/8/00, L. Cheng).

Samples of raw agricultural and processed commodities from the current crop field trials were analyzed for residues of pyraclostrobin and BF 500-3 using the LC/MS/MS method (BASF Method D9908, MRID 46710001 (currently under BEAD review)). Briefly, residues were extracted by shaking with methanol:water:2 N HCl (70:25:5; v:v:v) and centrifuged. Residues were then partitioned with cyclohexane, concentrated to dryness, and re-dissolved in buffered methanol:water (80:20, v:v). The final chromatographic analysis of residues was determined by LC/MS/MS. Total residues of pyraclostrobin and BF 500-3 are expressed as pyraclostrobin equivalents. For each analyte, the validated method LOQ is 0.02 ppm, and the estimated LODs are 0.003-0.03 ppm. The method is adequate for data collection based on acceptable concurrent method recovery data.

Analytical Methods - Livestock

Two methods have also been proposed for enforcing tolerances for livestock commodities: HPLC/UV method 439/0 and Method 446 (consisting of GC/MS method 446/0 and LC/MS/MS method 446/1). The HPLC/UV method determines residues of pyraclostrobin *per se*. Method 446 has a hydrolysis step, and determines residues of pyraclostrobin and its metabolites as BF 500-5 and BF 500-8. The validated method LOQs for BF 500-5 type residues, in parent equivalents, are 0.01 ppm for milk and 0.05 ppm for tissues, and the validated LOQs for BF 500-8 type residues, in parent equivalents, are 0.01 ppm for milk and 0.05 ppm for tissues. Independent method validation data for the HPLC/UV and LC/MS/MS methods are acceptable (D269668,

11/28/01, L. Cheng). Radiovalidation data submitted for the GC/MS and LC/MS/MS methods are adequate for liver and milk, and marginal for muscle. Method 446 has been forwarded to ACB/BEAD for petition method validation. As poultry tolerances are not currently necessary, an enforcement method for poultry commodities is not required at the present time.

Multiresidue Methodology (860.1360)

Data pertaining to the multiresidue methods testing of pyraclostrobin and its desmethoxy metabolite were reviewed (PP#0F6139, D269668, 11/28/01, L. Cheng). Pyraclostrobin was successfully evaluated through several of the FDA protocols, while recovery of BF 500-3 was unsuccessful in all protocols. Pyraclostrobin was completely recovered through Protocol D (in grape) and E (in grape), and partially recovered through Protocol F (in peanut). Metabolite BF 500-3 had poor peak shape and inadequate sensitivity with Protocol C columns, and therefore, was not further analyzed under Protocol D, E, and F. The results of the multiresidue testing for pyraclostrobin were forwarded to FDA on 1/4/02 for the purpose of updating PAM, Volume I.

5.1.4 Storage Stability Data

Adequate storage stability studies are available indicating that pyraclostrobin and metabolite BF 500-3 are relatively stable at $\leq$-10°C in fortified samples of grape juice (juices), sugar beet tops (leafy vegetables), sugar beet roots (root crop), tomato (fruit/fruiting vegetable), wheat grain (non-oily grain) and wheat straw (dry feed) for up to 25 months, and in fortified samples of peanut nutmeats (oilseed) and peanut oil for up to 19 months (D269668, L. Cheng, 11/28/01).

Conclusions. There are adequate storage stability data from PP#0F6139 which may be translated in the current petitions to validate sample storage conditions and durations. There are no corrections which need to be applied as pyraclostrobin residues of concern were found to be relatively stable over a wide range of commodities under frozen storage conditions for 19-25 months.

5.1.5 Magnitude of the Residue in Plants

The field trials conducted on fresh herbs (basil, chives, and dill) and avocados included a tank mixture of the pyraclostrobin test formulation (BAS 500 02F) with another active ingredient, boscalid (formulated as BAS 510 UCF). The field trials conducted on oats also reflect a tank mixture with metconazole (formulated as BAS 555 01F). Only the residue data from treatments with pyraclostrobin are reported in this risk assessment.

Field Trial Data Submitted Under PP#6F7105
Canola -DER Reference: 46925301.der.doc

BASF Corporation has submitted field trial data for pyraclostrobin on canola. A summary of residue data from the canola field trials is presented in Table 4. The residue decline data indicate that residues of pyraclostrobin decrease at longer preharvest intervals.

Table 4. Summary of Residue Data from Canola Field Trials with Pyraclostrobin.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Combined Residue Levels of Pyraclostrobin and its Metabolite BF 500-3 (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Proposed use pattern: Four foliar sprays at 0.10 lb ai/A/application for a seasonal rate of 0.39 lb ai/A with a 21-day PHI.									
Canola seed	0.39-0.41	20-22	32	<0.04	0.27	0.25	0.05	0.08	0.06
	0.20	21-22	10	<0.04	0.11	0.10	0.04	0.06	0.03

Conclusions: The proposed use patterns of pyraclostrobin on canola and flax include foliar and seed treatments. The residue data included in the canola field study only reflect foliar use, and no seed treatment data were submitted. Based on the seeding rate typically used for canola (4-8 lb of seed per acre) and flax (28-84 lb of seed per acre), the proposed maximum seed treatment rate of 0.04 lb ai/100 lb of seed per acre would be equivalent to maximums of 0.012 lb ai/A for flax and 0.0032 lb ai/A for canola, which are negligible compared to the maximum proposed seasonal rate of ~0.4 lb ai/A for foliar uses.

The submitted field trial data reflecting foliar uses for canola seed are adequate. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500, and the conducted field trials reflect the maximum proposed foliar use pattern.

Oats - DER Reference: 46902226.der.doc

BASF Corporation has submitted field trial data for pyraclostrobin on oats. A summary of residue data from the oat field trials is presented in Table 5. The decline data show that pyraclostrobin residues remain relatively constant in oat commodities with increasing preharvest intervals.

Table 5. Summary of Residue Data from Oat Field Trials with Pyraclostrobin									
Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Combined Residue Levels of Pyraclostrobin and its Metabolite BF 500-3 (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Proposed use pattern: Two foliar sprays at 0.15 lb ai/A/application for a seasonal rate of 0.3 lb ai/A. The proposed PHIs are 14 days for hay and green chopped oats (forage). No PHIs are proposed for grain and straw.									
Grain	0.29-0.31	20-26	24	0.10	0.75	0.64	0.35	0.33	0.18
Straw			24	1.33	14.90	13.40	3.92	4.70	3.07
Hay	0.29-0.31	6-8	24	2.38	14.83	14.46	6.00	6.25	3.20

Conclusions: The proposed use patterns of pyraclostrobin on oats include foliar and seed treatments. The supporting residue data included in the current petition only reflect foliar use, and no seed treatment data were submitted. Based on the seeding rate typically used for oats (50-120 lb of seed per acre), the proposed seed treatment rate of 0.005-0.01 lb ai/100 lb of seed per acre would be equivalent to 0.005-0.012 lb ai/A which is negligible compared to the maximum proposed seasonal rate of ~0.3 lb ai/A for foliar use.

The submitted field trial data reflecting foliar uses for oat grain, straw, and hay are adequate to fulfill data requirements pending submission of revised Sections B and F. Based on the available data, a revised Section B is required to specify PHIs of 20-26 days for oat grain and straw and 6-8 days for oat hay. A revised Section F is required to amend the proposed tolerances as determined by the Agency's tolerance spreadsheet.

Geographic representation of residue data for oat grain, straw, and hay is not in full compliance with GLN 860.1500 requirements since only 12 trials were conducted; the guideline requires a total of 16 trials to establish individual tolerances for oat commodities. However, the petitioner has included Appendix J in the study report which documents correspondence between EPA and BASF regarding the "Proposal to EPA and PMRA for Reduction of the Number of Field Residue Sites Required to Set a Fungicide Tolerance in Small Grains (Wheat, Barley, Oats, and Rye)". Based on the total number of field trials conducted for small grains, it was reported that the conducted trials for oats should be adequate to set individual tolerances on wheat, barley, oats, and rye.

No residue data are submitted for oat forage. The petitioner did not provide residue data or propose a tolerance for oat forage because applications are made after the growth stages at which oat is foraged. Based on the current proposed use patterns, the Agency will not require residue data or a tolerance for oat forage.

The field trial data for oat grain, straw, and hay were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels. The tolerance spreadsheet recommends tolerances of 1.2 ppm for oat grain, 15 ppm for oat straw, and 18 ppm for hay. These recommended levels vary slightly from the petitioner's tolerance proposals of 1.0 ppm for oat grain and 17 ppm each for oat hay and straw.

Field Trial Data Submitted Under PP#6E7165

Herbs subgroup 19A

Basil - DER Reference: 47014803.der.doc

IR-4 has submitted field trial data for pyraclostrobin on basil. A summary of residue data from the basil field trials is presented in Table 6. The processing of fresh basil to dried basil resulted in an increase of total residues, and the calculated processing factors of total residues ranged 4.6-9.0x with an average factor of 6.5x.

Table 6. Summary of Residue Data from Basil Field Trials with Pyraclostrobin.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Combined Residue Levels of Pyraclostrobin and its Metabolite BF 500-3 (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Proposed use pattern: Two foliar sprays at 0.15 lb ai/A/application for a seasonal rate of 0.3 lb ai/A with a 0-day PHI.									
Fresh basil	0.80-0.83	0	8	7.2	21.1	16.1	8.9	10.9	4.5
		3-4	8	1.3	7.5	7.4	4.9	4.8	2.6
Dried basil		0	4	40.1	80.6	80.6	74.7	67.5	18.5

Chives - DER Reference: 47014802.der.doc

IR-4 has submitted field trial data for pyraclostrobin on chives. A summary of residue data from the chive field trials is presented in Table 7.

Table 7. Summary of Residue Data from Chive Field Trials with Pyraclostrobin.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Combined Residue Levels of Pyraclostrobin and its Metabolite BF 500-3 (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Proposed use pattern: Two foliar sprays at 0.15 lb ai/A/application for a seasonal rate of 0.3 lb ai/A with a 0-day PHI.									
Chives	0.81-0.83	0	8	0.7	8.8	7.8	6.9	5.8	3.1

Dill - DER Reference: 47014801.der.doc

IR-4 has submitted field trial data for pyraclostrobin on dill. A summary of residue data from the dill field trials is presented in Table 8.

Table 8. Summary of Residue Data from Dill Field Trials with Pyraclostrobin.									
Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Combined Residue Levels of Pyraclostrobin and its Metabolite BF 500-3 (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Proposed use pattern: Two foliar sprays at 0.15 lb ai/A/application for a seasonal rate of 0.3 lb ai/A with a 0-day PHI.									
Fresh Dill	0.81-0.82	0	8	3.98	19.54	19.01	9.66	10.46	5.79
Dill Seed	0.80-0.83	0	6	3.60	22.60	21.20	18.30	14.45	8.34

Conclusions: The submitted residue data for basil (fresh and dried) and chives, the representative commodities of Herbs subgroup 19A, along with those data submitted for dill (fresh and seed) are adequate with respect to geographic representation of data. However, the field trials were conducted at an exaggerated total application rate of ~0.8 lb ai/A (2.7x the maximum proposed seasonal rate of 0.3 lb ai/A). As a result, these data are not indicative of the magnitude of the residue following applications at the proposed use pattern.

The petitioner has submitted a product label for Pristine® Fungicide and this supplemental label directions state, "Do not apply more than 37 oz/A per season", which equals 0.3 lb pyraclostrobin. HED, at times, allows a revised Section B to reflect this different rate. However, the proposed formulation contains two active ingredients, i.e., pyraclostrobin (12.8%) and boscalid (25.2%). A review of the boscalid data (See memo of 11/27/2007, C. Olinger), shows that boscalid was applied only twice but by using a different formulation, for a total of 0.59 lb a.i./A. This matches the proposed use rate for boscalid. If applied at the proposed label rate for pyraclostrobin (2 applications/season, 0.3 lb ai/A/season), then boscalid would be applied at the proposed rate (2 applications/season, 0.58 lb ai/A/season). However, if this combined formulation is applied at the exaggerated rate as representative of the submitted field trials, pyraclostrobin would be applied at 0.8 lb/ai/A/season, while boscalid would be applied at 1.58 lb ai/A/season (2.7x). Although the recommended pyraclostrobin tolerance would cover any pyraclostrobin residues at four (4) applications/season, boscalid residues at this treatment rate would probably exceed the recommended tolerance for boscalid. Thus, if it is the intent of the petitioner to propose this combined formulation for herbs (subgroup 19A), then a simple label revision will not solve the problem. The data only support two (2) applications of boscalid, and not four (4) applications. The proposed label cannot be revised to match the submitted pyraclostrobin residue field trial data.

Residue decline data were not submitted and are not required for the purpose of this petition since GLN 860.1500 states that decline data will typically not be required for each minor crop needing three or fewer total trials to establish an individual tolerance.

The field trial data for all fresh herbs (basil, chives, and dill) reflecting the exaggerated rate were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine an appropriate tolerance level. The tolerance spreadsheet recommends a tolerance of 25.0

ppm for Herbs subgroup 19A. This tolerance level is slightly lower than the level (30.0 ppm) initially proposed by the petitioner. Additional data from the basil and dill field trials suggest that tolerances are needed for dried basil leaves at 85 ppm and dill seed at 25 ppm. Based on the above discussion, this recommended tolerance would be higher than needed when the proposed label directions (2 applications/season) are followed.

Avocado - DER Reference: 47014804.der.doc

IR-4 has submitted field trial data for pyraclostrobin on avocados. A summary of residue data from the avocado field trials is presented in Table 9.

Table 9. Summary of Residue Data from Avocado Field Trials with Pyraclostrobin.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Combined Residue Levels of Pyraclostrobin and its Metabolite BF 500-3 (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Proposed use pattern: Two foliar sprays at 0.15 lb ai/A/application for a seasonal rate of 0.3 lb ai/A with a 0-day PHI.									
Avocado	0.73-0.78	0	14	0.08	0.48	0.40	0.16	0.18	0.11

Conclusions: The submitted residue data for avocado are inadequate to fulfill data requirements because the field trials were conducted at exaggerated rates. Not only were the individual application rates higher than the label maximum, but two additional applications beyond what is specified on the label were applied, resulting in a seasonal application rates ~2.5 – 2.7x the maximum proposed seasonal label rate. While the submitted data represent an overestimate of the residues expected from the proposed use, the degree of exaggeration can not be determined. The use of the proportionality concept (See CHEMSAC, minutes, 05/09/2007) to adjust residues downward is not considered appropriate since the data included more applications than the desired use. Given that the proposed use is for late season foliar application, and includes a 0-day preharvest interval, for the purpose of this IR-4 petition, HED will use the submitted data to support a tolerance for avocado. However, since HED considers that the tolerance may need to be reduced, and further since this data is being translated to support a wide number of tropical/subtropical fruits, HED requests that the petitioner provide an additional two to three field trials at the label rate (2 applications, total 0.3 lb ai/season) as a condition of registration.

The field trial data for avocado reflecting the exaggerated rate were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine an appropriate tolerance level. The tolerance spreadsheet recommends a tolerance of 0.6 ppm for avocado which is slightly lower than the level (0.7 ppm) initially proposed by the petitioner.

The submitted data for avocado may be translated to other tropical fruits for which uses are proposed pending label revision as specified above. HED is in the process of revising the Commodity Definitions listed under 40 CFR §180.1(h) to make the

tropical/subtropical fruit avocado a general commodity; see 6/14/06 memo by B. Schneider entitled "Reviewer's Guide and Summary of HED ChemSAC Approvals for Amending Crop Groups/Subgroups [40 CFR §180.41] and Commodity Definitions [40 CFR §180.1(h)]". The specific commodities included in the general definition for avocado include black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple. Until the regulations have been finalized in the Federal Register, separate tolerances are needed for each specific commodity, at the same level as the respective general commodity tolerance. Therefore, the petitioner is required to submit a revised Section F to propose a tolerance of 0.6 ppm for each of the following commodities: avocado, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple.

Field Trial Data Submitted Under PP#7E7245

Barley - DER Reference List 47190501.der.doc

IR-4 has submitted field trial data for pyraclostrobin on barley. A summary of residue data from the barley field trials is presented in Table 10.

Table 10. Summary of Residue Data from Barley Field Trials with Pyraclostrobin

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Combined Residue Levels of Pyraclostrobin and its Metabolite BF 500-3 (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Proposed use pattern: Two foliar sprays at 0.15 lb ai/A/application for a seasonal rate of 0.3 lb ai/A with a 14-day PHI.									
Grain	0.29-0.30	14-15	8	0.54	0.98	0.93	0.85	0.80	0.16
Straw			8	1.7	4.0	3.8	2.8	2.7	0.79
Grain	0.29-0.30	21-23	8	0.11	0.49	0.45	0.39	0.34	0.14
Straw			8	0.65	2.2	1.8	1.4	1.3	0.50

Conclusions: The submitted field trial data for barley grain and straw are adequate to fulfill data requirements pending submission of a revised Section F to amend the proposed tolerances as determined by the Agency's tolerance spreadsheet.

Geographic representation of residue data for barley grain and straw are adequate. No residue data were submitted for barley forage, and these data are normally required to support the amended use pattern. However, the petitioner did not provide residue data or propose a tolerance for barley hay because applications are made after the growth stages at which barley hay is harvested. Based on the current proposed use patterns, the Agency will not require residue data or a tolerance for barley hay.

The field trial data for barley grain and straw were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels. The tolerance spreadsheet recommends tolerances of 1.4 ppm for barley grain and 6.0 ppm for barley straw. These

recommended levels vary slightly from the petitioner's tolerance proposals of 1.3 ppm for barley grain and 9.0 ppm for barley straw.

Amended Registration Request for At Planting Use on Corn, Soybean & Sugar Beet
BASF Corporation submitted a supplemental label to add an in-furrow spray application at planting for corn, soybean and sugar beet onto the Headline® label (EPA Reg. No. 7969-186) at 0.2 lb ai/acre and a maximum seasonal of 0.29 lb ai/acre. Currently, Headline® is registered for foliar use on corn, soybean and sugar beet. No residue data reflecting in-furrow at planting applications were submitted. However, based on the confined accumulation studies in rotational crops and field rotational crop studies, HED determined (DP Barcode 340585, L. Cheng, 9/13/07) that the established tolerances in/on corn, soybean and sugar beet commodities will be adequate to cover the proposed supplemental use pattern and no new residue data are needed.

5.1.6 Magnitude of the Residue in Processed Food/Feed

Basil - Residue data on dried basil leaves are included and summarized in the Magnitude of the Residue section for fresh basil.

Barley - No residue data for the barley processed commodities (bran and pearled) are submitted. However, data from the wheat processing studies (MRID #'s 45118620 and 45321101) can be translated to adequately support the proposed use on barley. Based on the wheat studies, residues are not expected to concentrate in barley processed commodities.

Canola - DER Reference: 46925301.de1.doc

BASF Corporation has submitted a processing study with pyraclostrobin on canola. A summary of residue data from the canola processing study is presented in Table 11. The results indicate that the combined residues of pyraclostrobin and its metabolite BF 500-3 averaged 0.05 ppm in/on canola seed treated at a total rate of 1.2 lb ai/A. Following processing, combined residues were <0.04 ppm in meal and 0.06 ppm in refined oil. The equivalent processing factors from these data are 0.8x for meal and 1.2x for refined oil. The maximum theoretical concentration factors for canola processed commodities, based on separation into components, are 1.9x for meal and 3.0x for oil (OPPTS GLN 860.1520, Table 3).

Table 11. Residue Data from Canola Processing Study with Pyraclostrobin.							
RAC	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Combined Residues of Pyraclostrobin and its BF 500-3 Metabolite (ppm)			Processing Factor
				Pyraclostrobin	BF-500-3	Combined	
Canola seed	Seed	1.2	21	0.02, 0.03	<0.02, <0.02	<0.04, 0.05	--
	Meal			<0.02, 0.03	<0.02, <0.02	<0.04, <0.04	0.8x
	Refined oil			0.04, 0.04	0.02, 0.03	0.05, 0.07	1.2x

Conclusions: The canola processing study is acceptable to satisfy data requirements. The treated samples of canola seed (RAC) used for processing bore average combined residues of 0.05 ppm. Following processing of the RAC, total residues concentrated marginally in refined oil (1.2x) but reduced in meal (0.8x). The maximum expected combined residues in refined oil, resulting from the proposed use, is 0.3 ppm. This value was calculated by multiplying the processing factor of 1.2x by the HAFT residue of 0.25 ppm (see Table 4). The maximum expected residue in refined oil is identical to the recommended tolerance for the RAC (canola seed). Based on this determination, tolerances need not be established for the processed commodities of canola.

Oat - No residue data for the oat processed commodities (flour and groats/rolled oats) are submitted. However, data from the wheat processing studies (MRID #'s 45118620 and 45321101) can be translated to adequately support the proposed use on oat. Based on the wheat studies, residues are not expected to concentrate in oat processed commodities.

5.1.7 Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

Livestock dietary burdens

The potential for secondary transfer of pyraclostrobin residues of concern in meat, milk, poultry, and eggs exists because there are several livestock feedstuffs (canola meal, oat grain, oat forage, oat straw, and oat hay) that are associated with the proposed uses in the current petitions. The livestock dietary burdens of pyraclostrobin are presented in Table 12, and reflect the most recent guidance from HED concerning revisions of feedstuff percentages in Table 1 Feedstuffs (October 2006) and constructing reasonably balanced livestock diets (RBDs). The calculated dietary burdens of pyraclostrobin are 4.7 for beef cattle, 11.9 ppm for dairy cattle, 1.0 ppm for poultry, and 0.2 ppm for swine.

Table 12. Livestock Dietary Burdens for Pyraclostrobin[a].

Feedstuff	Type	Tolerance, ppm	% Dry Matter	% Diet [b]				Residue (ppm)			
				Beef	Dairy	Poultry	Swine	Beef	Diary	Poultry	Swine
almond hulls	R	1.6	90	-	5	-	-	-	0.89	-	-
barley, hay (oat, hay)	R	25 (18)	88	10	5	-	-	2.8	2.8 (1.0)	-	-
corn, field, forage (silage)	R	5.0	40	-	30	-	-	-	3.8	-	-
cotton gin byproducts	R	30.	90	5	-	-	-	1.7	-	-	-
legume, hay (cowpea)	R	25	30	-	5	-	-	-	4.2	-	-
barley, grain	CC	0.4	88	20	20	10	20	0.09	0.09	0.08	0.08
corn, field, grain	CC	0.1	88	50	20	-	65	0.057	0.023		0.065
oat, grain	CC	1.2	88	-	-	70	-	-	-	0.84	-
cotton, undelinted seed	PC	0.3	85	-	15	-	-	-	0.049	-	-
sunflower/canola (meal)	PC	0.3	92	15	-	20	15	0.049	-	0.06	0.045
Totals				100	100	100	100	**4.7**	**11.9 (10.1)**	**1.0**	**0.2**

[a] All data are based on Table 1 Feedstuffs (October 2006), a revision of feedstuffs data found in Table 1 (180.1000 OPPTS Test Guidelines). Residue levels for beef and dairy are corrected for moisture content and are determined by formula: tolerance / %DM x % in diet. Residue levels for poultry and swine are considered "as-is" and are determined by formula: tolerance x % in diet. R: roughage; CC: carbohydrate concentrate; PC: protein concentrate.

[b] Typical compositions of daily rations for the animals of choice for Table 1 data follow:

Feedlot beef have a daily ration of 15-40 % R, 45-80 % CC, and 10-15 % PC. As the slaughter time (last 3 months) gets closer, then the beef cattle are fed higher amounts of CC (up to 80 %), and lower amounts of R (15-20 %) and PC (5-10 %). The average life span for feedlot beef is 16-18 months Most of feedlot beef are slaughtered in 4 major centers located in the Midwest and the processed meat is "boxed" and shipped to distributors for sale to local grocers. Commercial ground beef (75-93 % lean) is produced from the combination of feedlot beef (60-70 % lean) and other lean meat sources, i.e., beef cows and bulls from cow-calf operations, imported lean meat trimmings, and replacement non-lactating dairy cows.

High volume milk-producing lactating dairy cows have a daily ration of 45 % R, 40-45 % CC, and 10-15 % PC. Dairy cows usually produce 2-3 calves before slaughter. The average life span of the lactating dairy cow is 3-4 years. Upon slaughter, much of the meat is used in ground beef and processed foods e.g., deli meats, soups, frozen dinners/entrees.

A laying hen that will give a steady egg production is fed 75-80 % CC and 20-25 % PC. The life span can be up to 18 months. In general, laying hens are not processed and marketed as whole or cut-up chickens. Much of the layer meat is used in processed food products, e.g., deli meats, soups, canned chicken, etc. (Note: The laying hen is the animal of choice. Frying and rotisserie chickens come from the broiler, a fast food chicken, weighing 3.5-4.0 lb.), and an animal that is raised in a very short time. The average life span is 38-42 days. The broiler diet contains 85-90 % CC and 10-15 % PC.

A marketable hog diet that will give steady growth would have 80-85 % CC and 15-20 % PC. Most of the US hog production is confined to "mega" operations. Animals are born in in-house nurseries, and simply moved to connecting buildings as the animal grows until slaughter (250 lb finished animal in 6 months). These animals provide meat for the "fresh pork" market.

Note: These guidelines are not to be used for pesticide residues that bioaccumulate. Contact Health Effects Division, OPP, EPA for these types of pesticides.

Animal feeding studies

Residue Chemistry Memo, DP# 269668, 11/28/01, L. Cheng (PP#0F6139)

Adequate feeding studies were reviewed in PP#0F6139. The current pyraclostrobin tolerances for livestock commodities were established based on results from these studies and the Agency's estimated dietary burdens for pyraclostrobin residues, which were originally calculated to be 36.3 ppm for beef cattle, 35.4 ppm for dairy cattle, and 0.35 ppm for poultry.

In the ruminant feeding study, dairy cows were dosed orally for 28 days with pyraclostrobin at levels equivalent to 8.8 ppm (0.7x the recalculated dietary burden), 27.2 ppm (2.3x), and 89.6 ppm (7.5x) in their diet. The study results from the 27.2 ppm-dose level were reproduced from the initial petition review and are presented in below Table 13.

Table 13. Residues of pyraclostrobin and its metabolites hydrolyzable to BF 500-5 and BF 500-8 in milk and tissues from cows dosed twice daily with pyraclostrobin at levels equivalent to 27.2 ppm for 28 consecutive days.

Dosing or Sampling Day	Mid Dose (27.2 ppm)			
	HPLC/UV Method 439	GC/MS (milk) Method 446/0 or LC/MS/MS (tissues) Method 446/1		
	Pyraclostrobin *per se* (ppm)	Residues hydrolyzable to BF 500-5, ppm pyraclostrobin equivalents [1]	Residues hydrolyzable to BF 500-8, ppm pyraclostrobin equivalents [2]	Total residues, ppm pyraclostrobin equivalents [3]
Whole Milk				
1	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.02, <0.02, <0.02
4	--	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.02, <0.02, <0.02
7	--	<0.01, <0.01, <0.01	<0.01, <0.01, 0.0124	<0.02, <0.02, <0.0224
10	--	<0.01, <0.01, <0.01	<0.01, <0.01, 0.011	<0.02, <0.02, <0.021
12	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.01, <0.01, 0.0119	<0.02, <0.02, <0.0219
15	--	<0.01, <0.01, <0.01	<0.01, 0.0126, 0.0135	<0.02, <0.0226, <0.0235
18	--	<0.01, <0.01, <0.01	<0.01, 0.0104, 0.0130	<0.02, <0.0204, <0.0230
21	--	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.02, <0.02, <0.02
24	--	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.02, <0.02, <0.02
27	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.01, <0.01, 0.0108	<0.02, <0.02, <0.0208
Skim Milk				
26	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.02, <0.02, <0.02
Milk Fat				
26	<0.01, <0.01, <0.01	<0.01, <0.01, <0.01	<0.01, 0.0368, 0.0461	<0.02, <0.0468, <0.0561
Fat				
29	<0.05, <0.05, <0.05	<0.05, <0.05, <0.05	<0.05, <0.05, <0.05	<0.1, <0.1, <0.1
Kidney				
29	<0.05, <0.05, <0.05	<0.05, <0.05, <0.05	<0.05, <0.05, <0.05	<0.1, <0.1, <0.1
Liver				

Table 13. Residues of pyraclostrobin and its metabolites hydrolyzable to BF 500-5 and BF 500-8 in milk and tissues from cows dosed twice daily with pyraclostrobin at levels equivalent to 27.2 ppm for 28 consecutive days.

Dosing or Sampling Day	Mid Dose (27.2 ppm)			
	HPLC/UV Method 439	GC/MS (milk) Method 446/0 or LC/MS/MS (tissues) Method 446/1		
	Pyraclostrobin *per se* (ppm)	Residues hydrolyzable to BF 500-5, ppm pyraclostrobin equivalents [1]	Residues hydrolyzable to BF 500-8, ppm pyraclostrobin equivalents [2]	Total residues, ppm pyraclostrobin equivalents [3]
29	<0.05, <0.05, <0.05	0.0645, 0.0761, 0.0973	0.399, 0.426, 0.510	0.464, 0.502, 0.607
Muscle				
29	<0.05, <0.05, <0.05	<0.05, <0.05, <0.05	<0.05, <0.05, <0.05	<0.1, <0.1, <0.1

[1] Pyraclostrobin and its metabolites hydrolyzable to BF 500-5 were determined in milk using the GC/MS method and in tissues using the LC/MS/MS method.
[2] Metabolites hydrolyzable to BF 500-8 were determined in milk using the GC/MS method and in tissues using the LC/MS/MS method.
[3] Total BF 500-5 and BF 500-8 residues, expressed as pyraclostrobin equivalents.

In the poultry feeding study, laying hens were orally dosed once daily for 30 consecutive days with pyraclostrobin at dose levels equivalent to 0.28 ppm (0.3x), 0.88 ppm (1.1x), and 3.01 ppm (3.0x). At the highest feeding level of 3.01 ppm, residues of pyraclostrobin and its metabolites hydrolyzable to BF 500-5 were less than the method LOQ (0.05 ppm) in all egg and tissue samples, except for one egg sample (Day 17) where residues of pyraclostrobin were detected at 0.064 ppm and <0.05 ppm upon re-analysis. Residue analysis of BF 500-8 was not conducted (the metabolism data show all metabolites hydrolyzable to BF 500-8 would be less than 10% TRR), but instead an isomeric compound (BF 500-9) was measured. Levels of BF 500-9 also were all <0.05 ppm.

Conclusions: Based on these dietary exposure levels and the residue data from the ruminant feeding study, the existing pyraclostrobin tolerances for milk (0.1 ppm), meat (0.1 ppm), fat (0.1 ppm), meat byproducts except liver (0.2 ppm), and liver (1.5 ppm) of cattle, goats, hogs, horses, and sheep are adequate to support the proposed uses. Tolerances for eggs and poultry are not needed based on data from the poultry feeding and metabolism studies [Category 180.6(a)(3)]. If in the future, if a petitioner proposes a use which increases the dietary burdens of poultry, then the Category 3 situation will be re-evaluated.

5.1.8 Confined and Field Rotational Accumulation in Rotational Crops

An adequate confined rotational crop study is available on pyraclostrobin (PP#0F6139, D269668, L. Cheng, 11/28/01; D314519, L. Cheng, 05/05/05). The confined study indicates that the metabolism of pyraclostrobin in rotated crops is similar but more extensive than that in primary crops. Pyraclostrobin undergoes demethoxylation to yield BF 500-3, followed by further degradation to medium polar and polar metabolites, and subsequent conjugation reactions and incorporation into natural products. The MARC (D278044, L. Cheng, 10/09/01) concluded that the residues of concern in rotational crops consist of pyraclostrobin and metabolite BF 500-3.

An adequate limited field rotational crop study is available (PP#0F6139, D269668, L. Cheng, 11/28/01) reflecting six broadcast foliar applications of pyraclostrobin (EC) to cucumber at 0.19-0.20 lb ai/A/application and RTIs of 6-8 days, for a total of 1.2 lb ai/A/season. This rate is 1x the maximum use rate of any rotated crop. Average residues of pyraclostrobin and BF 500-3 were each <LOQ in/on RAC samples from all representative rotational crops (radish, cabbage and wheat) planted 14 days following the final application to the primary crop. These data indicate that the label specified 14-day plant-back restriction is acceptable for all crops that are not registered for direction application.

5.1.9 Drinking Water Residue Profile

Reference: *Tier II Drinking Water Assessment for the use of Pyraclostrobin (P.C. Code: 099100) on Oats and Oilseed (canola and flax) (Headline Fungcide); Corn, Soybean, and Sugar beets (Headline Fungcide); Fresh Herbs (crop group 19) and Tropical Fruits (avocado, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple) (Pristine Fungicide); and Turf and Ornamentals (Insignia Fungicide) (DP Barcodes 336190, 340588, 342584). G. Rothman, 9/6/07.*

The Environmental Fate and Effects Division (EFED) reviewed the proposed use rates associated with the Section 3 requests for the use of pyraclostrobin on oats and oilseed crops (canola and flax), fresh herbs (crop group 19), and tropical fruits (avocado, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple). Additionally, EFED reviewed the proposal to add aerial applications to existing turf and ornamentals use sites and the proposal to add in-furrow use to the existing corn, soybean, and sugar beets use sites.

This assessment was based on the application of the highest seasonal use rate (proposed or registered) of pyraclostrobin. The aerial application on turf and ornamentals contains the highest seasonal application at 0.5 lbs a.i./acre with 6 maximum seasonal applications at 14 day intervals. The proposed use rate for the aerial application on turf and ornamentals is the same as for the registered use of pyraclostrobin for ground application on turf (please see the,"Environmental Fate and Ecological Risk Assessment for the Registration of Pyraclostrobin", submitted February 6, 2002.). However, EFED believes that the aerial use of pyraclostrobin on turf and ornamentals will pose the upper-bound concentrations in surface and ground water since spray drift increases and application efficiency decreases in an aerial application technique.

Measures of exposure for pyraclostrobin in the drinking water assessment were obtained through modeling efforts only, since national-scale monitoring data were not identified. The Tier II drinking water assessment was performed using the Tier II PRZM/EXAMS (PE4V01 perl shell with PRZM 3.12 beta dated 5/24/01 and EXAMS version 2.98, 7/18/02) to assess surface water. Ground water concentrations were estimated using a Tier I SCI-GROW model (version 2.3, May 16, 2006) since a Tier II model has not been developed to assess ground water.

Acute effects of pyraclostrobin residues in drinking water are expressed in annual peak one-in-ten year concentrations, chronic effects in annual average one-in-ten year concentrations, and cancer effects in 30-year average concentrations. The upper-bound Tier II modeling predicts that the concentrations of pyraclostrobin in surface water are not likely to exceed 35.6 µg/L for the peak concentration, 2.3 µg/L for the annual average concentration, and 1.5 µg/L for the 30-year average concentrations. The SCI-GROW model predicts the acute and chronic concentrations of pyraclostrobin in shallow ground water to be 0.02 µg /L (0.02 ppb).

5.1.10 Proposed Tolerances

For purposes of both the tolerance expression and dietary risk assessment, HED has concluded that the residues of concern in plant commodities include pyraclostrobin and its desmethoxy metabolite, BF 500-3 (D278044, L. Cheng, 10/9/01), and the residues of concern in livestock commodities include pyraclostrobin and its metabolites convertible to 1-(4-chlorophenyl)-1H-pyrazol-3-ol (BF 500-5) and 1-(4-chloro-2-hydroxyphenyl)-1H-pyrazol-3-ol (BF 500-8).

Pyraclostrobin tolerances for plant commodities are listed in 40 CFR §180.582 (a)(1) and are expressed in terms of the combined residues of the fungicide pyraclostrobin (carbamic acid, [2-[[[1-(4-chlorophenyl)-1H- pyrazol-3-yl]oxy]methyl]phenyl]methoxy-, methyl ester) and its desmethoxy metabolite (methyl N-[[[1-(4-chlorophenyl)-1H-pyrazol-3-yl]oxy]methyl]phenyl carbamate), expressed as parent compound.

Pyraclostrobin tolerances for animal commodities are listed in 40 CFR §180.582 (a)(2) and are expressed in terms of the combined residues of the fungicide pyraclostrobin and its metabolites convertible to 1-(4-chlorophenyl)-1H-pyrazol-3-ol and 1-(4-chloro-2-hydroxyphenyl)-1H-pyrazol-3-ol, expressed as parent compound.

The tolerance expression proposed by BASF in PP#6F7105 is consistent with the tolerance definition for plant commodities listed in 40 CFR §180.582 (a)(1). The tolerance expression proposed by IR-4 in PP#6E7165 is expressed as pyraclostrobin *per se* and should be amended to include all pyraclostrobin residues of concern.

The petitioner, BASF Corp., is currently proposing a crop group tolerance of 0.4 ppm for "Oilseed, group 20". According to a 6/14/06 memo by B. Schneider entitled "Reviewer's Guide and Summary of HED ChemSAC Approvals for Amending Crop Groups/Subgroups [40 CFR §180.41] and Commodity Definitions [40 CFR §180.1(h)]", the new Oilseed Crop Group 20 is being established to harmonize with Canada's Crop Group 20. The representative commodities for the crop group are rapeseed (canola varieties only) and sunflower seed. Flax seed, for which uses are being proposed as part of this petition, is a member of this crop group. The memo further states that until the Federal Register Notice is published revising the Crop Group Regulation to establish the Oilseed Crop Group 20, tolerances for the representative commodities [rapeseed (canola seed) and sunflower seed] as well as all members of the crop group will be listed individually, and the tolerances will be identical.

The submitted residue data for canola seed are adequate and indicate that the maximum combined residues were 0.27 ppm in/on samples treated at 1x. An individual pyraclostrobin tolerance for sunflower has already been established at 0.3 ppm in 40 CFR §180.582. Although adequate residue data have been submitted and a tolerance of 0.3 ppm has been established for sunflower seed, the other representative member of the new Oilseed Crop Group 20, a crop group tolerance will not be appropriate at this time until the Federal Register is issued revising the Crop Group Regulation to establish the Oilseed Crop Group 20. The field trial data for canola seed were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels. The tolerance spreadsheet recommends a tolerance of 0.45 ppm for canola seed. Based on the submitted field trial data, HED is recommending individual tolerances of 0.45 ppm for all oilseeds in 3 subgroups: 1) rapeseed (i.e., borage, crambe, cuphea, echium, flax seed, gold of pleasure, hare's ear mustard, lesquerella, lunaria, meadowfoam, milkweed, mustard seed, oil radish, poppy seed, rapeseed, sesame, and sweet rocket); 2) sunflower (i.e., Castor oil plant, Chinese tallowtree, Euphorbia, Evening primrose, Jojoba, Niger seed, Rose hip, Safflower, Stokes aster, Sunflower, Tallowwood, Tea oil plant, Vernonia); 3) cotton (only entry presently in this subgroup). The canola seed data will be translated to all oilseeds in the rapeseed subgroup, and the sunflower data will be translated to all oilseeds in the sunflower subgroup. The petitioner is required to submit a revised Section F to propose individual tolerances for all above oilseeds at 0.45 ppm each.

The submitted field trial data for oat grain, straw, and hay are adequate pending label revision to specify PHIs of 20-26 days for oat grain and straw and 6-8 days for oat hay. The field trial data for oat grain, straw, and hay were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels. The tolerance spreadsheet recommends tolerances of 1.2 ppm for oat grain, 15 ppm for oat straw, and 18 ppm for hay. The petitioner did not provide residue data or propose a tolerance for oat forage because applications are made after the growth stages at which oat is foraged. Based on the current proposed use patterns, the Agency will not require residue data or a tolerance for oat forage.

The submitted field trial data for basil (fresh and dried) and chives, the representative commodities of Herbs subgroup 19A, along with those data submitted for dill (fresh and seed) are inadequate because the trials were conducted at an exaggerated rate of ~0.8 lb ai/A (2.7x). The submitted data may, however, be used to support the recommended subgroup tolerance. The field trial data for all fresh herbs (basil, chives, and dill) reflecting the exaggerated rate were entered into the Agency's tolerance spreadsheet to determine an appropriate tolerance level. The tolerance spreadsheet recommends a tolerance of 25.0 ppm for Herbs subgroup 19A. Additional data from the basil and dill field trials suggest that tolerances are needed for dried basil leaves at 85 ppm and dill seed at 25 ppm. However, a withdrawal letter for withdrawal of the fresh herbs section of petition #6E7165 has recently been received by OPP. Therefore, at this time HED is not recommending for tolerances on any herbs in the Herbs subgroup 19A.

The submitted field trial data for avocado are inadequate because the trials were conducted at an exaggerated rate (~2.6x) and no residue decline data were submitted. The submitted data may, however, be used to support the proposed tolerance for avocado. The field trial data for avocado reflecting the exaggerated rate were entered into the Agency's tolerance spreadsheet to determine an appropriate tolerance level. The tolerance spreadsheet recommends a tolerance of 0.6 ppm for avocado. Because of the exaggerated rate, the recommended tolerance would probably be higher than needed.

The submitted data for avocado may be translated to other tropical fruits (black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple) for which uses are proposed pending label revisions. HED is in the process of revising the Commodity Definitions listed under 40 CFR §180.1(h) to make the tropical/subtropical fruit avocado a general commodity. The specific commodities included in the proposed general definition for avocado include black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple. Until the regulations have been finalized in the Federal Register, separate tolerances are needed for each specific commodity, at the same level as the respective general commodity tolerance.

The submitted field trial data for barley grain and straw are adequate. The field trial data for barley grain and straw were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels. The tolerance spreadsheet recommends tolerances of 1.4 ppm for barley grain and 6.0 ppm for barley straw. No residue data were submitted for barley forage, and these data are normally required to support the amended use pattern. However, the petitioner did not provide residue data or propose a tolerance for barley hay because applications are made after the growth stages at which barley hay is harvested. Based on the current proposed use patterns, the Agency will not require residue data or a tolerance for barley hay.

An acceptable canola processing study has been submitted, and the results suggest that no tolerances are required for the processed commodities of canola. An oat processing study is required to support the proposed use on oats.

An acceptable limited field rotational crop study is available. No rotational crop tolerances are required pending label revision to specify a plantback interval of 14 days for all annual crops that are not registered.

Adequate cattle and poultry feeding studies are available. The existing pyraclostrobin tolerances for milk, meat, fat, meat byproducts except liver, and liver of cattle, goats, hogs, horses, and sheep were reassessed, and no adjustments are needed. Tolerances for eggs and poultry are not needed at this time based on data from the poultry feeding and metabolism studies [Category 180.6(a)(3)].

The Codex Alimentarius Commission has established maximum residue limits (MRLs) for residues of pyraclostrobin at 0.5 ppm for oats and at 0.05 ppm for papaya (see

Appendix I). The US tolerance level and residue definition both differ from Codex. There are no Canadian or Mexican MRLs for pyraclostrobin for the crop commodities discussed in this Summary Document.

A summary of the recommended tolerances for the crop commodities discussed in this document is presented in Table 14. The petitioner should submit a revised Section F reflecting the recommended tolerances and commodity definitions presented in Table 14.

Table 14. Tolerance Summary for Pyraclostrobin.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Tolerances Proposed Under PP#6E7105			
Oats grain	1.0	1.2	Tolerance recommendations are tentative pending submission of a revised Section B to specify PHIs of 20-26 days for oat grain and straw and 6-8 days for oat hay. *Oat, grain; oat, hay, and oat straw.*
Oats, hay	17	18	
Oats, straw	17	15	
Oilseed, group 20	0.4	Canola, seed at 0.45 Flax, seed at 0.45	A crop group tolerance will not be appropriate at this time until the Federal Register is issued revising the Crop Group Regulation to establish the Oilseed Crop Group 20. In the interim, HED is recommending individual tolerances on all oilseeds to be listed in the rapeseed subgroup.
Tolerances Proposed Under PP#6E7165			
Avocado	0.7	0.6	Tolerance recommended, but additional field trial data required as a condition of registration.
Tolerances Proposed Under PP#7E7245			
Barley, grain	1.3	1.4	Adequate field trial data are available on barley based on regional use.
Barley, straw	9.0	6.0	
Sapote, black	0.7	0.6	Tolerance recommendations are based on residue data translated from avocado.
Canistel	0.7	0.6	
Sapote, mamey	0.7	0.6	
Mango	0.7	0.6	
Papaya	0.7	0.6	
Sapodilla	0.7	0.6	
Star Apple	0.7	0.6	
Additional Tolerances That Need to be Proposed Under PP#6E7105			
Borage, Crambe, Cuphea, Echium, Flax seed, Gold of pleasure, Hare's ear mustard, Lesquerella, Lunaria, Meadowfoam, Milkweed, Mustard seed, Oil radish, Poppy seed, Rapeseed, Sesame, Sweet rocket (rapeseed subgroup); Castor oil plant, Chinese tallowtree, Euphorbia, Evening primrose, Jojoba, Niger seed, Rose hip, Safflower, Stokes aster Sunflower, Tallowwood, Tea oil plant, Vernonia (sunflower subgroup); Cotton (cotton subgroup)	none	0.45	HED is recommending individual tolerances on all oilseeds to be listed in the rapeseed subgroup.

5.2 Dietary Exposure and Risk

Reference: *Pyraclostrobin. Acute and Chronic Aggregate Dietary and Drinking Water Exposure and Risk Assessments to Support New Use on Oat Grain, Barley Grain, Oilseed (Crop Group 20), Fresh Herbs (Herbs Subgroup 19A), Avocado, Black Sapote, Canistel,*

Mamey Sapote, Mango, Papaya, Sapodilla, and Star Apple. PC Code: 099100; Decision Number: 370224; DP Number: 348308; S. Piper; 02/11/08.

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. The risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). HED is concerned when estimated dietary risk exceeds 100% of the PAD.

DEEM-FCID™ Program and Consumption Information

Pyraclostrobin acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.03), which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. For chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups, but for acute exposure assessment are retained as individual consumption events. Based on analysis of the 1994-96, 98 CSFII consumption data, which took into account dietary patterns and survey respondents, HED concluded that it is most appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (i.e., only those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for

all tiers of analysis. However, for tiers 1 and 2, any significant differences in user vs. per capita exposure and risk are specifically identified and noted in the risk assessment.

Drinking Water Inputs

The drinking water residues used in the dietary risk assessment were provided by EFED in the following memorandum: "*Tier II Drinking Water Assessment for the use of Pyraclostrobin (P.C. Code: 099100) on Oats and Oilseed (canola and flax) (Headline Fungcide); Corn, Soybean, and Sugar beets (Headline Fungcide); Fresh Herbs (crop group 19) and Tropical Fruits (avocado, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple) (Pristine Fungicide); and Turf and Ornamentals (Insignia Fungicide) (DP Barcodes 336190, 340588, 342584). G. Rothman, 9/6/07*" and incorporated directly into this dietary assessment. EFED selected the proposed aerial application on turf and ornamentals as the use site to base their drinking water assessment upon, since it provided the highest seasonal use rate (proposed or registered) of pyraclostrobin (0.5 lbs a.i./acre with 6 maximum seasonal applications at 14 day intervals). Additionally, EFED believes that the aerial use of pyraclostrobin on turf and ornamentals will pose the upper-bound concentrations in surface and ground water since spray drift increases and application efficiency decreases in an aerial application technique.

The drinking water assessment provides Tier II (PRZM 3.12/EXAMS 2.98) surface water modeling and Tier I (SCI-GROW, version 2.3) groundwater modeling. The modeling was conducted for the parent compound only. The residue concentrations from Tier II surface water modeling are not expected to exceed 35.6 µg/L for the peak concentration, 2.3 µg/L for the annual average concentration, and 1.5 µg/L for the 30 year average concentration. Residue concentration from Tier I groundwater modeling is not expected to exceed 0.02 µg/L. For acute exposures the 35.6 µg/L peak concentration was used. For chronic exposures the 2.3 µg/L annual average concentration was used. These drinking water residues were incorporated in the DEEM-FCID into the food categories "water, direct, all sources" and "water, indirect, all sources."

Residue Data Used for Acute and Chronic Assessments

For the acute dietary analysis, tolerance level or highest field trial residues were used for all crops. The crops for which the highest field trial residues were used are as follows: Amaranth, leafy; Arugula; Chrysanthemum; Cress, garden; Cress, upland; Dandelion, leaves; Fennel; Parsley, leaves; Radicchio; Rhubarb; Spinach; Swiss chard; Beans, dry; Celery; Lettuce, head; Lettuce, leaf; and Pea, dry. One hundred percent crop treated was assumed for all commodities in the assessment. For the chronic dietary analysis, anticipated residues were derived for certain crops (apple, broccoli, celery, collard, grape, lettuce, citrus, pepper, mustard green and tomato), which are the major dietary contributors based on preliminary runs. Experimentally derived processing factors for apple juice, grape juice, citrus juices, tomato paste, tomato puree, wheat flour, and wheat germ were applied.

Results of Acute Dietary Exposure Analysis

The results of the aggregate acute dietary analysis for food and water indicate that acute dietary risks do not exceed Agency's level of concern (< 100% of the aPAD) for the U.S. population and all subgroups. At the 95th percentile, the U.S. population has an exposure from food and drinking water that results in a risk estimate for the general U.S. population at 1% of the aPAD. The most highly exposed subpopulation is "females 13-49 years" at 80% of the aPAD. The results of the acute dietary exposure analysis at the 95th percentile of exposure are reported in Table 15 below.

Results of Chronic Dietary Exposure Analysis

The results of the aggregate chronic dietary analysis for food and drinking water indicate that chronic dietary risks (food and drinking water) do not exceed HED's level of concern (<100% cPAD) for the U.S. population and all subgroups. The U.S. population exposure from food and water results in a risk estimated at 19% of the cPAD. The most highly exposed population subgroup is "children 1 -2" with an exposure estimated at 48% of the cPAD. The results of the chronic dietary exposure analysis are reported in Table 15, below.

Table 15. Summary of Dietary Exposure and Risk for Pyraclostrobin – Food & Water

	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
Population Subgroup	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	0.043	1.4	0.0061	19	A separate quantitative cancer risk assessment is not required.	
All Infants (< 1 year old)	0.055	1.8	0.011	33		
Children 1-2 years old	0.072	2.4	0.016	**48**		
Children 3-5 years old	0.064	2.2	0.012	36		
Children 6-12 years old	0.046	1.5	0.0074	22		
Youth 13-19 years old	0.035	1.2	0.0043	13		
Adults 20-49 years old	0.039	1.3	0.0050	15		
Adults 50+ years old	0.041	1.4	0.0057	17		
Females 13-49 years old	0.040	**80**	0.0047	14		

Conclusions

Acute and chronic exposures and risks do not exceed HED's level of concern for the U.S. population and for all relevant population subgroups. Since risk estimates are below HED's level of concern, a more highly refined analysis is not needed at this time. Of note is that contribution from drinking water is minimal. HED concludes that the acute

and chronic exposure estimates are unlikely to underestimate actual acute or chronic exposure.

5.3 Anticipated Residue and Percent Crop Treated (%CT) Information

The acute analysis was conducted using tolerance level residues or the highest residues for all commodities. These tolerance level or highest residues were derived from field trial data conducted at the maximum application rate and minimum PHI permitted on the proposed or existing labels. For all commodities 100% crop treated was assumed. A limited number of experimentally derived processing factors were used to refine the acute and chronic analyses.

The chronic dietary assessment was conducted using tolerance level residues for all crops except for apple, celery, grape, head lettuce, leaf lettuce, orange, pepper, spinach, tomato and additional crops in the leafy vegetables group where anticipated average residue values were derived from crop field trials. These field trials represent maximum application rates and minimum PHIs. For all commodities 100% crop treated was assumed.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

A product containing pyraclostrobin (i.e., Insignia®) is registered for application to residential turf grass and recreational sites. It may be applied to turf at rates ranging from 0.28 to 0.5 lb ai/A, at intervals of 14 to 28 days; and the maximum seasonal application rate is 3 lb ai/A. The residential exposure assessment was prepared in an HED memorandum dated 8/19/04 (D298017, K. O'Rourke). Residential and recreational turf applications are applied by professional pest control operators (PCOs) only, and therefore, residential handler exposures do not occur. There is, however, a potential for exposure to homeowners in residential settings from entering previously treated lawns where children might play and adults might work or play. As a result, risk assessments have been completed for postapplication scenarios. The short-term MOEs for each postapplication scenario resulted in MOEs above 100, and therefore are not of concern. For toddlers, the short-term dermal MOE is 180 (0.027 mg/kg/day) and the combined incidental oral MOE is 620 (0.009425 mg/kg/day; hand-to-mouth activities), and combined dermal and oral exposures result in and MOE of 140. Dermal and incidental oral exposures are combined because they share common toxic effects; i.e., decreased body weight gain and decreased food intake/efficiency. For adults, the short-term dermal MOE is 260 (0.019 mg/kg/day).

Recreational exposures to turf are expected to be similar to, or in many cases less than, those evaluated for residential postapplication exposure and risk; and therefore, a separate recreational exposure assessment was not conducted.

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for pyraclostrobin. The Agency has been working with the Spray Drift Task

Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

7.0 Aggregate Risk Assessments and Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures from various sources, HED considers both the route and duration of exposure. Common effects (i.e., decreased body weight gain, food intake, and food efficiency) were seen in the studies selected to evaluate dietary, dermal and incidental oral ingestion exposures; and therefore, route-specific exposures can be aggregated.

Based on the proposed Section 3 food crop uses, aggregate assessments were conducted for acute and chronic dietary exposures (food + drinking water), and existing short-/intermediate-term residential exposures (i.e., chronic dietary, plus incidental oral and dermal exposures for kids, and chronic dietary, plus dermal exposures for adults). Both short- and intermediate-term exposures may occur during postapplication activities for adults and children. However, because the toxicity endpoints and points of departure are identical for short- and intermediate-term exposures, separate risk estimates for short- and intermediate-term exposures were not calculated.

To assess aggregate acute and chronic dietary risks, estimates of pesticide residues in drinking water (EDWCs) were incorporated directly into the dietary exposure analysis. **Refer to section 5.2 for these risk estimates.**

The short-/intermediate-term aggregate risk assessment takes into account average exposure estimates from dietary consumption of pyraclostrobin (food and drinking water) and non-occupational/residential uses (turf). Postapplication exposures from the use on turf are considered predominantly short-term (1-30 days). To calculate the short-/intermediate-term aggregate risk estimates, the chronic dietary exposure (food + drinking water) is added to the residential exposures using the inverse MOE methodology described below (see Table 16 below). The total combined MOE from dietary (food + water) and non-occupational/residential exposure is 100 for children 1-2 years old, which is not of concern to HED. For adults the total combined MOE is 200, which also is not of concern to HED. These aggregate exposure risk assessments are considered conservative

estimates, that should not underestimate risks, because of the following inputs: 1) dietary inputs primarily used tolerance level residues; 2) crop specific (turf) screening level drinking water modeling data were used (i.e., Tier II surface water model); 3) maximum application rates and minimum application intervals were used; and 4) conservative SOPs and upper level estimates of exposure were employed.

Table 16. Short-/Intermediate Term Aggregate Risk Calculations

Population	Dermal Exposure			Oral Exposure				Total Combined MOE[2]
	NOAEL mg/kg/day	Exposure mg/kg/day	MOE[1]	NOAEL mg/kg/day	Incidental Oral Exposure mg/kg/day	Chronic Dietary (Food + Water) mg/kg/day	MOE[1]	
Children 1-2 yrs	5	0.027	180	5.8	0.009425	0.0164	220	100
Adults	5	0.019	260	5	NA	0.00613	820	200

[1] The Level of Concern MOE is 100.

[2] Total Combined MOE = $1/ [(1/MOE_{Dermal}) + (1/MOE_{Oral})]$

8.0 Cumulative Risk Characterization/Assessment

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to pyraclostrobin and any other substances and pyraclostrobin does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that pyraclostrobin has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

9.0 Occupational Exposure/Risk Pathway

Reference: *Pyraclostrobin: Occupational and Residential Risk Assessment to Support Request for Section 3 Registrations on Oats and Oilseed Crop group (Foliar and Seed Treatment), Herbs, and Tropical Fruits. (DP#: 348792; PC#: 099100) K. O'Rourke; 01/31/08.*

9.1 Short-/Intermediate-Term Handler Risk

Foliar and In-Furrow Treatment

Occupational handlers may experience short-/intermediate-term exposure to pyraclostrobin while mixing/loading and applying sprays to agricultural crops. No

chemical-specific handler exposure data were submitted in support of this use pattern. It is the policy of the HED to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 as presented in PHED Surrogate Exposure Guide (8/98) to assess handler exposures when chemical-specific monitoring data are not available (HED Science Advisory Council for Exposure Draft Policy # 7, dated 1/28/99).

The results of the occupational handler exposure and risk assessment indicate that risks are not of concern with baseline clothing, or in some cases, when gloves and respirator are used to mitigate exposure. [Note: The respirator unit exposure value represents a PF 5 NIOSH-approved filtering face-piece respirator (e.g., dust mask), which is considered to provide an 80% reduction in inhalation exposure.] Exposure assumptions and MOE estimates are summarized in Table 17.

It is feasible for the same individual to mix/load and apply formulations, especially for groundboom and airblast applications, however, appropriate data are not available in PHED for which unit exposures for these combined activities can be derived. HED does not recommend simply adding the unit exposure values for each job function because any extrapolation error (i.e., exposure from the amount ai handled in the study to that of a real-life application) would be magnified, leading to greater uncertainty. For information and characterization purposes, even with the over-estimation uncertainty, the MOEs for these combined activities for groundboom and airblast application of pyraclostrobin would be above the LOC of 100, and not of concern (i.e., dermal/inhalation MOEs of 1,400/210 and 1,200/510, respectively).

The proposed Headline® Fungicide label requires chemical resistant gloves, however, a respirator is not indicated. In addition, the minimum level of PPE for handlers is based on acute toxicity for the end-use products. The Registration Division (RD) is responsible for ensuring that PPE listed on the label is in compliance with the Worker Protection Standard (WPS).

Table 17. Summary of MOEs for Occupational Handlers of Pyraclostrobin (Foliar Treatment)

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai) [1]	Inhalation Unit Exposure (mg/lb ai) [1]	Use Site	Application Rate (lb ai/A) [2]	Area Treated (A/day) [3]	Daily Dose (mg/kg/day) [4]		Short-/Int-term MOE [5]	
						Dermal	Inhalation	Dermal	Inhalation
Mixer/Loader									
(1) Mixing/Loading Liquid for Aerial application or Chemigation	2.9 or 0.023 (w/gloves)	0.0012 or 0.00024 (w/ respirator)	Oats	0.15	1,200	1.2 0.0097 (gloves)	0.0031 0.00062 (respirator)	4.1 520 (gloves)	75 370 (respirator)
			Canola & Flax	0.10	350	0.24 0.0019 (gloves)	0.00060	21 2,700 (gloves)	380
(2) Mixing/Loading Liquid for Groundboom application or Chemigation			In-Furrow tmt	0.20	200	0.27 0.0021 (gloves)	0.00069	18 2,300 (gloves)	340
			Oats	0.15	200	0.20 0.0016 (gloves)	0.00051	25 3,100 (gloves)	450
			Canola & Flax	0.10	80	0.054 0.00043 (gloves)	0.00014	92 12,000 (gloves)	1,700
(3) Mixing/Loading Dry Flowables for Aerial application or Chemigation	0.066	0.00077	Turf & Ornamentals	0.50	350	0.027	0.0019	190	120
			Herbs & Tropical Fruit	0.15	350	0.0081	0.00058	620	400

Table 17. Summary of MOEs for Occupational Handlers of Pyraclostrobin (Foliar Treatment)

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai) [1]	Inhalation Unit Exposure (mg/lb ai) [1]	Use Site	Application Rate (lb ai/A) [2]	Area Treated (A/day) [3]	Daily Dose (mg/kg/day) [4]		Short-/Int-term MOE [5]	
						Dermal	Inhalation	Dermal	Inhalation
(4) Mixing/Loading Dry Flowables for Groundboom application			Herbs	0.15	80	0.0018	0.00013	2,700	1,700
(5) Mixing/Loading Dry Flowables for Airblast application			Tropical Fruit	0.15	40	0.00092	0.000066	5,400	3,500
Applicator									
(6) Applying Sprays with Fixed-wing Aircraft	0.005	0.000068	Turf & Ornamentals	0.50	350	0.0020	0.00017	2,400	1,400
			Oats	0.15	1,200	0.0021	0.00017	2,400	1,300
			Herbs & Tropical Fruit	0.15	350	0.00061	0.000051	8,200	4,500
			Canola & Flax	0.10	350	0.00041	0.000034	12,000	6,800
(7) Applying Sprays with Open Cab Groundboom	0.014	0.00074	In-Furrow tmt	0.20	200	0.0013	0.00042	3,800	540
			Oats	0.15	200	0.00098	0.00032	5,100	730
			Herbs	0.15	80	0.00039	0.00013	13,000	1,800
			Canola & Flax	0.10	80	0.00026	0.000085	19,000	2,700
(8) Applying Sprays with Open Cab Airblast Sprayer	0.36	0.0045	Tropical Fruit	0.15	40	0.0050	0.00039	990	600
Flagger									

Table 17. Summary of MOEs for Occupational Handlers of Pyraclostrobin (Foliar Treatment)									
Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai) [1]	Inhalation Unit Exposure (mg/lb ai) [1]	Use Site	Application Rate (lb ai/A) [2]	Area Treated (A/day) [3]	Daily Dose (mg/kg/day) [4]		Short-/Int-term MOE [5]	
						Dermal	Inhalation	Dermal	Inhalation
(9) Flagging to Support Aerial Applications	0.011	0.00035	Turf & Ornamentals	0.50	350	0.0045	0.00088	1,100	260
			Oats, Herbs & Tropical Fruit	0.15	350	0.0013	0.00026	3,700	880
			Canola & Flax	0.10	350	0.00090	0.00018	5,600	1,300

[1] Dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; values representing the addition of chemical-resistant gloves are shown for those scenarios in which the MOEs do not reach 100 at baseline. Inhalation unit exposure values represent no respirator, except for "Oats" in Scenario #1, for which a dust-mist respirator was added. Values are reported in the PHED Surrogate Exposure Guide dated August 1998.

[2] Application rates are based on maximum values found in proposed labels (See Table 1)

[3] Daily area treated is based on the area that can be reasonably applied in a single day for each exposure scenario, based on the application method and formulation/packaging type. (standard EPA/OPP/HED values).

[4] Daily Dose (mg/kg/day) = (Unit Exposure * % Absorption * Application rate * Area treated) / Body Weight of 60-kg for dermal or 70-kg for inhalation; where dermal absorption is 14%..

[5] Short-/Intermediate-Term MOE = NOAEL / Daily Dose. The dermal NOAEL is 5 mg/kg/day, and the inhalation NOAEL is 0.23 mg/kg/day. The LOC is 100.

Seed Treatment

Occupational handlers may experience short-/intermediate-term exposure to pyraclostrobin while performing seed treatment activities, including several distinct handling activities, each with its own exposure potential. These activities are: (1) loader/applicator; (2) sewer; (3) bagger; (4) multiple activities (including cleaning and forklift operation); and, (5) seed planters.

No chemical-specific handler exposure data were submitted in support of this use pattern. For assessing seed treatment activities, unit exposure data were taken from HED Science Advisory Council for Exposure Policy 14: Standard Operating Procedures for Seed Treatment. The amount of ai handled depends on the application rate (lb ai/100 lb seed) and the pounds of seed treated in a day (or the pounds of seed that can be planted in a day), all of which may vary, depending upon the seed type. Values for the amount of seed treated and planted per day were obtained from HED's Standard Operating Procedure (SOP) #15. Exposure and risk estimates for seed treatment handlers were calculated based on canola data (commercial rate assumed to be 718,000 lb seed/day) for seed treatment, and flax data for seed planting, which represent the maximum combination of application rate and amount handled for the proposed crops. The results are presented in Table 18.

For the proposed seed treatment uses, all seed treatment activities result in MOEs greater than the LOC of 100 with baseline clothing, or baseline plus gloves and respirator, and therefore, are not of concern. While there is a data gap for on-farm seed treatment (i.e., the data available for on-farm seed treatment represents a dust formulation in a planter box, which is not applicable) this scenario is not likely to result in risks of concern because seed treatment activities in the commercial setting (estimated in Table 18), which handle much greater quantities of seed, are not of concern. [Note: The respirator unit exposure value represents a PF 5 NIOSH-approved filtering face-piece respirator (e.g., dust mask), which is considered to provide an 80% reduction in inhalation exposure.]

The proposed BAS 500 ST label is a supplemental label only, and does not provide information regarding personal protective equipment (PPE) (i.e., whether gloves and a respirator are currently required). In addition, the minimum level of PPE for handlers is based on acute toxicity for the end-use product. The Registration Division (RD) is responsible for ensuring that PPE listed on the label is in compliance with the Worker Protection Standard (WPS).

Table 18. Summary of MOEs for Seed Treatment Activities

Activity	Dermal Unit Exposure (mg/lb ai) [1]	Inhalation Unit Exposure (mg/lb ai) [1]	Application Rate (lb ai/ lb seed) [2]	Seed Handled per Day (lb seed) [3]	Daily Dose (mg/kg/day) [4]		Short-/Int-term MOE [5]	
					Dermal	Inhalation	Dermal	Inhalation
Loader/ Applicator	0.023 (w/gloves)	0.00034	0.0004	718,000	0.015	0.0014	320	160
Sewer	0.0062	0.00023			0.0042	0.00094	1,200	240
Bagger	0.0091	0.00016			0.0061	0.00066	820	350
Multiple Activity	0.042 (w/gloves)	0.0016 or 0.00032 (w/respirator)			0.028	0.0066 or 0.0013 (w/respirator)	180	35 or 180 (w/respirator)
On-Farm	No data	No data		6,700	--	--	--	--
Seed Planter	0.25 (w/gloves)	0.0034			0.0016	0.00013	3,200	1,800

[1] Dermal unit exposure values represent baseline clothing (long pants, long sleeved shirts, shoes, and socks), except where gloves are indicated (for planting, gloves are for loading only). Inhalation unit exposure values represent no respirator, except for "multiple activity" scenario. There is a data gap for on-farm seed treatment; the formulation is a water-dispersible granule for which the label indicates standard slurry or mist-type seed treatment equipment should be used. The data available for on-farm seed treatment represents a dust formulation in a planter box scenario, which is not applicable.

[2] Application rates are based on maximum values in proposed seed treatment label (See Table 1)

[3] Values for amount of seed handled for all activities are based on an assumed rate for canola, except the on-farm and planter scenarios, which were based on flax.

[4] Daily Dose (mg/kg/day) = (Unit Exposure * % Absorption * Application rate * Seed Handled) / Body Weight of 60-kg for dermal or 70-kg for inhalation; where dermal absorption is 14%.

[5] Short-/Intermediate-Term MOE = NOAEL / Daily Dose. The dermal NOAEL is 5 mg/kg/day, and the inhalation NOAEL is 0.23 mg/kg/day. The LOC is 100.

9.2 Short-/Intermediate-Term Postapplication Risk

This Section 3 action for pyraclostrobin involves foliar applications to agricultural crops. Therefore, postapplication exposure is possible for workers entering treated fields. Chemical-specific dislodgeable foliar residue (DFR) data had previously been submitted by the registrant to support earlier registration requests for food crops (MRID#s: 45118727, 45118724, 45118726, and 45118728 and 45118729). An overview of each study was provided in a previous assessment (D269670, K. O'Rourke, 9/30/2002); a summary of the results is provided in Table 19.

The DFR data were used to estimate restricted entry intervals (REIs) by extrapolating, where possible, to the proposed crops. It was found that the type of formulation used influences the DFR profile; therefore, DFR data for both the emulsifiable concentrate and water-dispersible granule formulations were considered. Average percent initial DFR values were calculated (i.e., 18% for emulsifiable concentrate and 20% for water-dispersible granule) and used to estimate surrogate residue values for each crop, according to its proposed formulation. Although uncertainties are introduced into the

assessment when crop-specific residues are used to estimate residues for other types of crops, it is believed to be more realistic than using default assumptions

In addition to these residue data, transfer coefficients (Tc) are used to relate the foliage residues to activity patterns (e.g., scouting) to estimate potential human exposure. The transfer coefficients used in this assessment are from an interim transfer coefficient policy developed by HED's Science Advisory Council for Exposure using proprietary data from the Agricultural Re-entry Task Force (ARTF) database (policy # 3.1).

The estimated short-/intermediate-term MOEs are presented in Table 20. The results of the postapplication exposure and risk assessment indicate that MOEs of 100 are achieved on Day 0 for all scenarios and, therefore, are not of concern.

The pyraclostrobin technical material has been classified in Toxicity Category III for acute dermal, primary eye irritation, and primary skin irritation. Per the Worker Protection Standard (WPS), a 12-hr restricted entry interval (REI) is required for chemicals classified under Toxicity Category III or IV. The proposed labels indicate an REI of 12 hrs, which is in compliance with the WPS.

Table 19. Summary of DFR Study Results

Crop	Location (state)	Formu-lation	Application Rate (lb ai/A)	Number of Apps.	Interval	r^2	Initial DFR (% of Appl. Rate)	Dissipation (% per day)	Half-life (days)
peaches	CA	WDG	0.12	5	7 days	0.84	22	2	27.8
peaches	GA	WDG	0.12	5	7 days	0.97	15	11	6
peaches	PA	WDG	0.12	5	7 days	0.94	22	9	7.7
Peaches Average							20	7	
strawberries	NC	WDG	0.18	5	7 days	0.77	26	15	4.2
strawberries	CA	WDG	0.18	5	7 days	0.98	25	15	4.4
strawberries	OR	WDG	0.18	5	7 days	0.91	12	13	4.9
Strawberry Average							21	14	
peanuts	NC	EC	0.25	5	14 days	0.91	18	26	2.3
peanuts	GA	EC	0.25	5	14 days	0.77	17	61*	0.74
peanuts	TX	EC	0.25	5	14 days	0.91	18	24	2.5
Peanuts Average							18	25*	
grapes	CA	WDG	0.18	3	14 days	0.97	22	6	11.1
grapes	WA	WDG	0.18	3	14 days	0.94	25	6	11.8
grapes	PA	WDG	0.18	3	14 days	0.82	14	4	15.6
Grapes WDG Average							20	5	

Table 19. Summary of DFR Study Results

Crop	Location (state)	Formu-lation	Application Rate (lb ai/A)	Number of Apps.	Interval	r^2	Initial DFR (% of Appl. Rate)	Dissipation (% per day)	Half-life (days)
grapes	CA	EC	0.18	3	14 days	0.95	14	9	7.4
grapes	WA	EC	0.18	3	14 days	0.9	22	9	7.5
grapes	PA	EC	0.18	3	14 days	0.79	12	5	13.9
grapes	CA	EC	0.15	6	10 days	0.9	6	6	12
grapes	NY	EC	0.15	6	10 days	0.92	28	6	11.2
grapes	WA	EC	0.15	6	10 days	0.9	24	4	17.3
Grapes EC Average							18	7	
EC Average							**18**	**13**	
WDG Average							20	9	

WDG = water dispersible granule
EC = emulsifiable concentrate
* The results from the Georgia site reflect uncharacteristically high rainfall during the monitoring period. This is not representative of typical conditions, therefore, the dissipation from this site was not included in the average.

Table 20. Summary of Estimated Postapplication MOEs for Foliar Treatments

Crop	Application Rate (lb ai/A) [1]	DAT [2]	DFR [3] ($\mu g/cm^2$)	TC [4] (cm^2/hr)	Activity [4]	Short-/Int-Term MOE [5]
Canola & Flax	0.10	0	0.20	100	Irrigating and scouting immature/low foliage plants	13,000
				1,500	Irrigating and scouting mature/high foliage plants	890
Oats	0.15	0	0.30	100	Irrigating and scouting immature/low foliage plants	8,900
				1,500	Irrigating and scouting mature/high foliage plants	590
Herbs		0	0.34	500	Irrigation, scouting, thinning, weeding immature plants	1,600
				1,500	Irrigating and scouting mature plants	530
				2,500	Hand harvesting, pruning, and thinning mature plants	320
Tropical Fruit		0	0.34	100	Propping	8,000
				1,000	Irrigation, scouting, weeding	800
				1,500	Harvesting, pruning, training, tying	530
				3,000	Thinning	270

[1] Maximum application rate indicated on proposed labels (see Table 1).
[2] DAT = Days after treatment needed to reach the LOC of 100; DAT 0 = the day of treatment, after sprays have dried; assumed to be approximately 12 hours.
[3] DFR ($\mu g/cm^2$) = Application rate (lb ai/A) x CF (4.54E+8 ug/lb) x CF (2.47E-8 A/cm^2) x Initial Fraction of ai Retained on the Foliage (from Table 19, used EC average [18%] for canola, flax and oats, and WDG average [20%] for herbs and tropical fruits).

[4] TC (cm^2/hr) = transfer coefficients and associated activities from ExpoSAC Policy Memo #003.1 "Agricultural Transfer Coefficients", 8/17/2000.
[5] MOE = MOE on the corresponding DAT. MOE = NOAEL / Daily Dose.
Daily Dose = [(DFR x TC x 14% Dermal absorption x 8-hr Exposure Time)] / [(CF: 1000 µg/mg) x (60-kg Body Weight)]
Short-/intermediate-term Dermal NOAEL = 5 mg/kg/day. The LOC is 100.

10.0 Data Needs and Label Recommendations

10.1 Residue Chemistry Data Needs and Label Recommendations

For Petition #6F7105

860.1500 Crop Field Trials

Oats: No residue data are submitted for oat forage. The petitioner did not provide residue data or propose a tolerance for oat forage because applications are made after the growth stages at which oat is foraged. Based on the current proposed use patterns, the Agency will not require residue data or a tolerance for oat forage.

860.1900 Field Accumulation in Rotational Crops

Label revisions are required to specify a 14-day plantback interval restriction for all annual crops that are not registered.

860.1550 Proposed Tolerances

The petitioner should submit a revised Section F reflecting the recommended tolerances and commodity definitions presented in Table 14.

The petitioner should submit a revised Section F to propose individual tolerances of 0.45 ppm for all oilseeds in subgroups rapeseed, sunflower, and cotton, as follows: 1) rapeseed (i.e., borage, crambe, cuphea, echium, flax seed, gold of pleasure, hare's ear mustard, lesquerella, lunaria, meadowfoam, milkweed, mustard seed, oil radish, poppy seed, rapeseed, sesame, and sweet rocket); 2) sunflower (i.e., Castor oil plant, Chinese tallowtree, Euphorbia, Evening primrose, Jojoba, Niger seed, Rose hip, Safflower, Stokes aster, Sunflower, Tallowwood, Tea oil plant, Vernonia); and 3) cotton (only entry presently in this subgroup).

Note: The existing tolerances on sunflower at 0.3 ppm and cotton, undelinted seed at 0.3 ppm should be removed from 40 CFR §180.582.

860.1520 Processed Food and Feed

Oats: No residue data for the oat processed commodities (flour and groats/rolled oats) are submitted. However, data from the wheat processing studies (MRID #'s 45118620 and 45321101) can be translated to adequately support the proposed use on oat. Based on the wheat studies, residues are not expected to concentrate in oat processed commodities.

Barley: No residue data for the barley processed commodities (bran and pearled) are submitted. However, data from the wheat processing studies (MRID #'s 45118620 and 45321101) can be translated to adequately support the proposed use on barley. Based on the wheat studies, residues are not expected to concentrate in barley processed commodities.

For Petition #6E7165

860.1500 Crop Field Trials

The submitted residue data for avocado are inadequate to fulfill data requirements because the field trials were conducted at exaggerated rates (ca 2.6x). Since the submitted data represent an overestimate of the residues expected from the proposed use, HED considers that the tolerance for avocado may need to be reduced. Also, since the proposed use is for late season foliar application, includes a 0-day preharvest interval, and these data are being translated to support a wide number of tropical/subtropical fruits, HED requests that the petitioner provide additional, bridging field trial data (i.e., two to three field trials at the proposed label rate of 2 applications, total 0.3 lb ai/season) as a condition of registration.

860.1900 Field Accumulation in Rotational Crops

Label revisions are required to specify a 14-day plantback interval restriction for all annual crops that are not registered.

860.1550 Proposed Tolerances

The petitioner should submit a revised Section F to correct the tolerance residue definition (parent + metabolite) and to make it consistent with the definition listed in 40 CFR §180.582 (a)(1). The revised Section F should also incorporate the recommended tolerances and commodity definitions presented in Table 14.

For Petition #7E7245

860.1500 Crop Field Trials

Barley: No residue data were submitted for barley forage, and these data are normally required to support the amended use pattern. However, the petitioner did not provide residue data or propose a tolerance for barley hay because applications are made after the growth stages at which barley hay is harvested. Based on the current proposed use patterns, the Agency will not require residue data or a tolerance for barley hay.

860.1520 Processed Food and Feed

Barley: Residue data for the barley processed commodities (pearled barley and bran) are normally required. However, data from the wheat processing studies (MRID #'s

45118620 and 45321101) can be translated to adequately support the proposed use on barley. Based on the wheat studies, residues are not expected to concentrate in barley processed commodities.

860.1900 Field Accumulation in Rotational Crops

Label revisions are required to specify a 14-day plantback interval restriction for all annual crops that are not registered.

860.1550 Proposed Tolerances

The petitioner should submit a revised Section F reflecting the recommended tolerances and commodity definitions presented in Table 14.

10.2 Occupational Label Recommendations

The proposed Headline® Fungicide label requires chemical resistant gloves; however, a respirator is not indicated and is needed for the handler scenario of mixing/loading liquids for aerial application or chemigation.

The proposed BAS 500 ST label is a supplemental label only, and does not provide information regarding personal protective equipment (PPE). Such PPE information should be added to the label. Gloves are needed for several seed treatment scenarios, and a respirator is needed for the multiple activity scenario.

11.0 International Residue Limit Status

The Codex Alimentarius Commission, Mexico and Canada have not established any maximum residue limits (MRLs) for residues of pyraclostrobin in or on raw agricultural commodities, although a variety of MRLs are pending in Canada. Therefore, there are no questions of compatibility of U.S. tolerances with International MRLs at the present time.

INTERNATIONAL RESIDUE LIMIT STATUS			
Chemical Name: methyl [2-[[[1-(4-chlorophenyl)-1*H*-pyrazol-3-yl]oxy]methyl]phenyl]methoxy carbamate	Common Name: Pyraclostrobin	☐ Proposed tolerances ☒ Reevaluated tolerance ☐ Other	Date: 12/20/07
Codex Status (Maximum Residue Limits)		U. S. Tolerances	
☐No Codex proposal step 6 or above ☐No Codex proposal step 6 or above for the crops requested		Petition Numbers: 6E7105, 6E7165, and 7E7245 DP#s: 334535, 336189, and 343754 Other Identifier:	
Residue definition (step 8/CXL): pyraclostrobin (fat soluble)		Reviewers/Branch: B. Cropp-Kohlligan, G. Otakie, J. Stokes / RRB4	
		Residue definition in PP#6E7105, PP#6E7165,and PP#7E7245: Combined residues of pyraclostrobin and BF 500-3, expressed as pyraclostrobin.	

Crop (s)	MRL (mg/kg)	Crop(s)	Recommended Tolerance (ppm)
Oats	0.5	PP#6E7105	
Papaya	0.05	Oats grain	1.2
Barley	0.5	Oats, hay	18
		Oats, straw	15
		Canola, seed	0.45
		Flax, seed	0.45
		Borage	0.45
		Crambe	0.45
		Cuphea	0.45
		Echium	0.45
		Flax seed	0.45
		Gold of pleasure	0.45
		Hare's ear mustard	0.45
		Lesquerella	0.45
		Lunaria	0.45
		Meadowfoam	0.45
		Milkweed	0.45
		Mustard seed	0.45
		Oil radish	0.45
		Poppy seed	0.45
		Rapeseed	0.45
		Sesame	0.45
		Sweet rocket	0.45
		Castor oil plant	0.45
		Chinese tallowtree	0.45
		Euphorbia	0.45
		Evening primrose	0.45
		Jojoba	0.45
		Niger seed	0.45
		Rose hip	0.45
		Safflower	0.45
		Stokes aster	0.45
		Sunflower	0.45
		Tallowwood	0.45
		Tea oil plant	0.45
		Vernonia	0.45
		Cotton	0.45
		PP#6E7165	
		Avocado	0.6
		Sapote, black	0.6
		Canistel	0.6
		Sapote, mamey	0.6
		Mango	0.6
		Papaya	0.6

INTERNATIONAL RESIDUE LIMIT STATUS			
Chemical Name: methyl [2-[[[1-(4-chlorophenyl)-1*H*-pyrazol-3-yl]oxy]methyl]phenyl]methoxy carbamate	Common Name: Pyraclostrobin	☐ Proposed tolerances ☒ Reevaluated tolerance ☐ Other	Date: 12/20/07
Codex Status (Maximum Residue Limits)		U. S. Tolerances	
☐No Codex proposal step 6 or above ☐No Codex proposal step 6 or above for the crops requested		Petition Numbers: 6E7105, 6E7165, and 7E7245 DP#s: 334535, 336189, and 343754 Other Identifier:	
Residue definition (step 8/CXL): pyraclostrobin (fat soluble)		Reviewers/Branch: B. Cropp-Kohlligan, G. Otakie, J. Stokes / RRB4	
		Residue definition in PP#6E7105, PP#6E7165,and PP#7E7245: Combined residues of pyraclostrobin and BF 500-3, expressed as pyraclostrobin.	

Crop (s)	MRL (mg/kg)	Crop(s)	Recommended Tolerance (ppm)
		Sapodilla	0.6
		Star Apple	0.6
		PP#7E7245	
		Barley, grain	1.4
		Barley, straw	6.0

Limits for Canada		**Limits for Mexico**	
☒No Limits ☐No Limits for the crops requested		☒No Limits ☐No Limits for the crops requested	
Residue definition:		Residue definition:	
Crop(s)	MRL (mg/kg)	Crop(s)	MRL (ppm)
Notes/Special Instructions:			

12.0 Appendix: Toxicity Profile

12.1 Appendix 1.: Pyraclostrobin Toxicology Requirements and Available Studies for Food Uses

Appendix 1: Pyraclostrobin Toxicology Requirements and Available Studies for Food Uses.

Test		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	Oral Subchronic (rodent)	yes	yes
870.3150	Oral Subchronic (dog)	yes	yes
870.3200	28-Day Dermal	yes	yes
870.3465	28-Day Inhalation	yes	yes
870.3700a	Developmental Toxicity (rat)	yes	yes
870.3700b	Developmental Toxicity (rabbit)	yes	yes
870.3800	Reproduction	yes	yes
870.4100a	Chronic Toxicity (rat)	yes	yes
870.4100b	Chronic Toxicity (dog)	yes	yes
870.4200a	Oncogenicity (rat)	yes	yes
870.4200b	Oncogenicity (mouse)	yes	yes
870.5100	Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5375	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5395	Mutagenicity—Micronecleus - mammalian	yes	yes
870.5550	Mutagenicity—Unscheduled DNA - mammalian	yes	yes
870.6100a	Acute Delayed Neurotox. (hen)	no	-
870.6100b	90-Day Neurotoxicity (hen)	no	-
870.6200a	Acute Neurotox. Screening Battery (rat)	yes	yes
870.6200b	90 Day Neuro. Screening Battery (rat)	yes	yes
870.6300	Develop. Neuro	no	-
870.7485	General Metabolism	yes	yes
870.7600	Dermal Penetration	yes	yes

12.2 Appendix 2.: Acute Toxicity Data on Pyraclostrobin Technical

Appendix 2. Acute Toxicity Profile:

Table 1. Acute Toxicity Data on Pyraclostrobin Technical

Study/ Species	MRID	Results	Toxicity Category
870.1100 Acute Oral, Rats	45118302	LD_{50} = > 5000 mg/kg	IV
870.1200 Acute Dermal, Rabbits	45118305	LD_{50} = >2000mg/kg	III
870.1300 Acute Inhalation, Rats	45118308	0.31 mg/L < LC_{50} < 1.07 mg/L	II
870.2400 Primary Eye Irritation, Rabbits	45118311	Moderate eye irritation; MAS 4.6/110	III
870.2500 Primary Skin Irritation, Rabbits	45118314	Moderate skin irritation; MAS 2.2/8.0	III
870.2600 Dermal Sensitization, Guinea pig	45118317	Not a skin sensitizer	N/A

12.3 Appendix 3.: Subchronic, Chronic and Other Toxicity Profile

Appendix 3. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
870.3100 90-Day oral toxicity (rat)	45118321 (1999) Acceptable/guideline 0, 50, 150, 500, 1000, 1500 ppm M: 0, 3.5, 10.7, 34.7, 68.8, 105.8 mg/kg/day; F: 0, 4.2 12.6, 40.8, 79.7,118.9 mg/kg/day	NOAEL = 10.7 mg/kg/day LOAEL = 34.7 mg/kg/day based on ↓body weight/ weight gain in males, ↓food intake (both sexes), ↑ relative liver wt and spleen wt in females and histopathology of duodenum and liver in males, and spleen in both sexes.
870.3100 90-Day oral toxicity (mouse)	45118320 (1999) Acceptable/guideline 0, 50, 150, 500, 1000, 1500 ppm M: 0, 9.2, 30.4, 119.4, 274.4, 475.5 mg/kg/day F:0, 12.9, 40.4, 162.0, 374.1, 634.8 mg/kg/day	NOAEL = 9.2 mg/kg/day LOAEL = 30.4 mg/kg/day based on ↓body weight/ weight gain in males, changes in clinical chemistry in both sexes (increased urea and decreased triglycerides), and increased incidences in females of lymph node apoptosis, thymus atrophy, and ulcer/erosion in the glandular stomach.
870.3150 90-Day oral toxicity (dog)	45118323 (1999) Acceptable/guideline 0, 100, 200, 450 ppm M: 0, 2.8, 5.8, 12.9 mg/kg/day F: 0, 3.0, 6.2, 13.6 mg/kg/day	NOAEL = 5.8 mg/kg/day LOAEL = 12.9 mg/kg/day based on ↑diarrhea, clinical chem. changes, and increased incidence of thickening/ mucosal hypertrophy of the duodenum in both sexes; body weight loss, and ↓food intake/efficiency in females.
870.3050 28-Day oral toxicity (rat)	MRID 45118322 (1999) Acceptable/guideline 0, 20, 100, 500, 1500 ppm M: 0, 1.8, 9.0, 42.3, 120.2 mg/kg/day F: 0, 2.0 9.6, 46.6, 126.3 mg/kg/day	NOAEL = 9.0 mg/kg/day LOAEL = 42.3 mg/kg/day based on changes in hematology parameters, increased absolute and relative spleen weight, histopathology in spleen and liver, in addition to increased duodenal mucosal hyperplasia in both sexes.
870.3200 28-Day dermal toxicity (rat)	45118324 (1999) Unacceptable/guideline (a higher dose could be tolerated and the limit dose is 1000 mg/kg/day) 0, 40, 100, 250 mg/kg for 5 days/wk	Dermal NOAEL = 40 mg/kg/day Dermal LOAEL = 100 mg/kg/day based on scale formation, hyperkeratosis, and epidermal thickening. Systemic NOAEL = 250 mg/kg/day Systemic LOAEL > 250 mg/kg/day The HIARC (TXR 0051553) determined that a repeat study at a higher dose is not needed since an oral end-point (developmental toxicity NOAEL of 5.0 mg/kg/day) with a 14% dermal absorption rate yields a dermal equivalent dose of 36 mg/kg/day (5 ÷ 0.14) which is well below the apparent systemic toxicity NOAEL of 250 mg/kg/day in the dermal study.

Appendix 3. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
870.3465 28-Day inhalation toxicity (rat)	46638801 (2005) Acceptable/guideline 0.001, 0.030, or 0.300 mg/L for 6 hours per day, 5 days/week (20 exposure days) – Test substance was dissolved in acetone and administered as an aerosol	Inhalation NOAEL = 0.001 mg/L (oral equivalent dose = 0.23 mg/kg/day) Inhalation LOAEL = 0.030 mg/L (oral equivalent dose = 6.9 mg/kg/day) based on findings of hyperplasia in the duodenum, alveolar histiocytosis in the lungs, and olfactory atrophy/necrosis in the nasal tissues.
870.3700a Prenatal developmental (rat)	45118325 (1999) Acceptable/guideline 0, 10, 25, 50 mg/kg/day	**Maternal** NOAEL = 10 mg/kg/day LOAEL = 25 mg/kg/day based on ↓body wt/ wt gain and ↓food intake/efficiency. **Developmental** NOAEL = 25 mg/kg/day LOAEL = 50 mg/kg/day based on ↑ incidences of dilated renal pelvis and cervical ribs with no cartilage.
870.3700b Prenatal developmental (rabbit)	45118326 and 45437001 (1999) Acceptable/guideline 0, 1, 3, 5, 10, 20 mg/kg/day	**Maternal** NOAEL = 5 mg/kg/day LOAEL = 10 mg/kg/day based on ↓ body wt gain and ↓food intake/efficiency. **Developmental** NOAEL = 5 mg/kg/day LOAEL =10 mg/kg/day based on ↑ resorption/post-implantation loss.
870.3800 Reproduction and fertility effects (rat)	**Two Generation**: MRID 45118327 (1999) Acceptable/guideline when combined with the one generation preliminary study (below) 0, 25, 75, 300 ppm F0 M/F: 0, 2.5/2.6, 7.4/7.8, 29.0/30.4 mg/kg/day F1 M/F: 0, 2.8/3.0, 8.6/9.0, 35.0/36.0 mg/kg/day **One Generation**: MRID 45596210 (2002) 0, 200, 400, 600 ppm F0 M/F: 0, 20.5/21.3, 39.9/42.5, 59.1/60.4 mg/kg/day	**Parental/Systemic** NOAEL = 29 mg/kg/day LOAEL > 29 mg/kg/day based on no effects. **Reproductive** NOAEL = 29 mg/kg/day LOAEL > 29 mg/kg/day based on no effects. **Offspring** NOAEL = 29 mg/kg/day LOAEL > 29 mg/kg/day based on no effects. **Offspring** NOAEL < 20.5 mg/kg/day **Offspring** LOAEL = 20.5 mg/kg/day based on decreased pup body weight and body weight gain on and after post-natal day 7.
870.4100a Chronic toxicity (rat)	45118329 (1999) Unacceptable/guideline 0, 25, 75, 200 ppm M: 0, 1.1, 3.4, 9.0 mg/kg/day F: 0, 1.5, 4.6, 12.3 mg/kg/day	NOAEL = 9.0 mg/kg/day LOAEL > 9.0 mg/kg/day.
870.4100b Chronic toxicity (dog)	45118328 (1999) Acceptable/guideline 0, 100, 200, 400 ppm M: 0, 2.7, 5.4, 10.8 mg/kg/day F: 0, 2.7, 5.4, 11.2 mg/kg/day	NOAEL = 5.4 mg/kg/day LOAEL = 10.8 mg/kg/day based on ↑ diarrhea and clinical chemistry changes in both sexes (decreased cholesterol, protein, albumin, and globulin), and ↓ body weight gain and ↓food intake/efficiency in females.

Appendix 3. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
870.4200 Carcinogenicity (rat)	45118331 (1999) Acceptable/guideline 0, 25, 75, 200 ppm M: 0, 1.2, 3.4, 9.2 mg/kg/day F: 0, 1.5, 4.7, 12.6 mg/kg/day	NOAEL = 3.4 mg/kg/day LOAEL = 9.2 mg/kg/day based on ↓ body weight and body weight gain, and kidney atrophy/tubular casts in both sexes; hepatic necrosis and gross/ microscopic ulcerations/lesions in the glandular and fore-stomachs in males. **No evidence of carcinogenicity**
870.4300 Carcinogenicity (mouse)	45118330 (1999) Unacceptable/guideline M: 0, 10, 30, 120 ppm 0, 1.4, 4.1, 17.2 mg/kg/day F: 0, 10, 30, 120, 180 ppm 0, 1.6, 4.8, 20.5, 32.8 mg/kg/day	NOAEL = M: 4.1 mg/kg/day F: 32.8 mg/kg/day LOAEL = M: 17.1 mg/kg/day based on decrease in body weight gain (20%) at 13 weeks which was supported by the results of a 90-day study. F >32.8 mg/kg/day Inadequate dosing in females based on CARC Report dated 10/22/03 (TXR # 0051445) **No evidence of carcinogenicity**
Gene Mutation 870.870.5100 Bacterial reverse mutation assay	45118332 (1997) Acceptable/guideline	**Negative** ± S9 up to 5,000 µg/plate by standard plate and tube preincubation. No cytotoxicity at any dose but there was precipitation at ≥2,500 µg/plate.
Gene Mutation 870.5300 Mammalian cell culture	45118335 (1998) Acceptable/guideline	**Negative** ± S9 up to cytotoxic and precipitating concentration of 20 µg/mL
Cytogenetics (*in vitro*) 870.5375 Chromosomal aberrations	45118333 (1999) Acceptable/guideline	**Negative** ± S9 for clastogenic/aneugenic activity up to 25 µg/mL. Precipitation and cytotoxicity (reduced cell attachment and poor quality of metaphases) were seen at concentrations ≥50 µg/mL.
Cytogenetics 870.5395 Micronucleus test in mouse	45118334 (1998) Acceptable/guideline	**Negative** for clastogenic/aneugenic activity up to the highest dose tested (300 mg/kg). In a preliminary study, doses ≥400 mg/kg caused death.
Unscheduled DNA synthesis 870.5550 Rat hepatocyte culture	45118336 (1998) Acceptable/guideline	**Negative** up to a cytotoxic concentration of 1.0 µg/mL.
870.6200a Acute neurotoxicity screening (rat)	45118337(1999) Acceptable/guideline 0, 100, 300, 1000 mg/kg	**Neurotoxicity** NOAEL = 1000 mg/kg M/F LOAEL >1000 mg/kg **Systemic** M/F NOAEL = 300/1000 mg/kg M/F LOAEL 1000/ >1000 mg/kg based on ↓body weight gain in males.

Appendix 3. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
870.6200b Subchronic neurotoxicity screening (rat)	45118401 (1999) Acceptable/guideline 0, 50, 250, 750 (M)/1500 (F) ppm M: 0, 3.5, 16.9, 49.9 mg/kg/day F: 0, 4.0, 20.4, 111.9 mg/kg/day	**Neurotoxicity** M/F NOAEL = 49.9/111.9 mg/kg/day M/F LOAEL >49.9/111.9 mg/kg/day. **Systemic** M/F NOAEL = 16.9/20.4 mg/kg/day M/F LOAEL = 49.9/111.9 mg/kg/day based on ↓ body weight gain, and ↓ food intake/efficiency.
870.7485 Metabolism and pharmacokinetics (rat)	45118403 (1998) 45118404 (1999) Acceptable/guideline	Nearly 35% of an oral dose of pyraclostrobin is absorbed with urinary and fecal excretions accounting for about 15% and 85%, respectively, and bile elimination accounted for about 30%. Two peak plasma concentrations were reached at 0.5-1 and 8 hours with lower plasma concentrations in males than females (by 16-38%) during the early peak phase. Elimination was biphasic at a low dose with plasma half lives of nearly 10/35 hours and monophasic at a high dose with a half-life of nearly 20 hours. Tissue distribution was fast, peaking at 0.5 hours, and was slightly higher among females. Some of the highest concentrations were found in the liver, thyroid, kidney, lung, adrenal glands, and pancreas but all levels dropped by more than 20-fold within 72 hours. About 33 metabolites were identified in urine, feces, and bile with no sex- or dose-related differences but the position of the label seemed to alter the profile, particularly in the urine. Desmethoxy pyraclostrobin (500M07) is one of the major metabolites in rat and is also found in large amounts in plants (BF 500-3) and livestock (500M07). The rat metabolic pathway included phase-I reactions such as N-demethoxylation, various hydroxylations, and cleavage of the ether bond with subsequent oxidation; these reactions were followed by phase II glucuronidation and sulfation.
870.7600 Dermal penetration (rat)	45118402 (1999) Unacceptable/guideline (most of the test material was retained on the dressing and was unavailable for absorption; therefore, actual dose cannot be determined.	The HIARC calculated and recommended a dermal penetration rate of 14% (report dated 2/10/03; TXR # 0051553)